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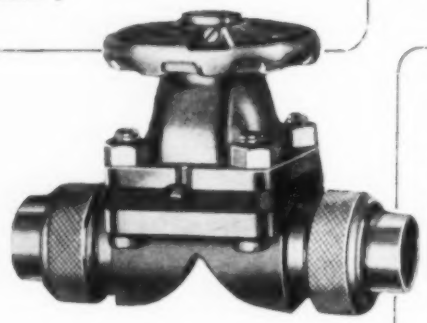

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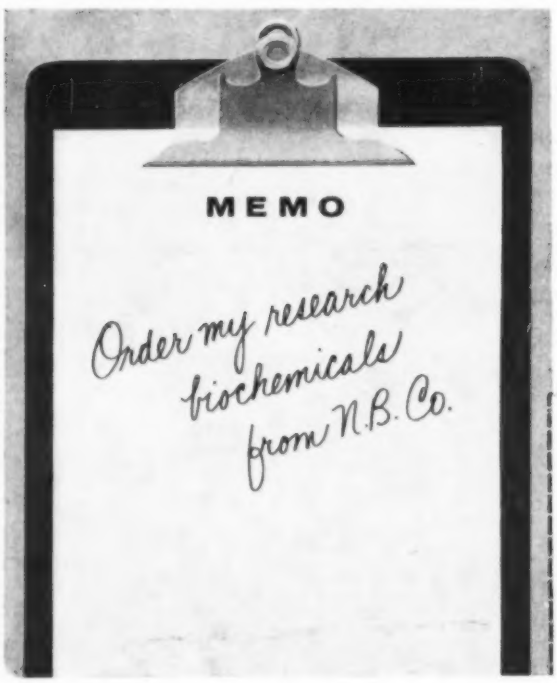

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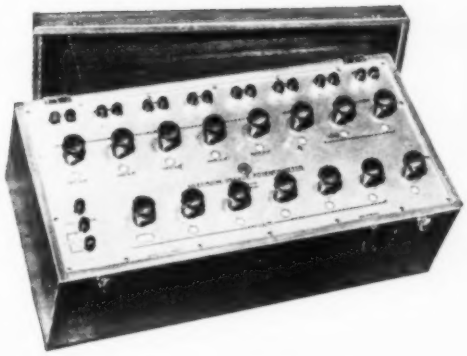

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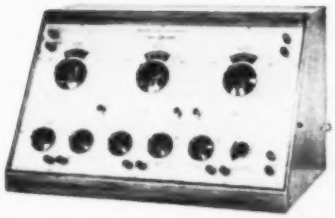

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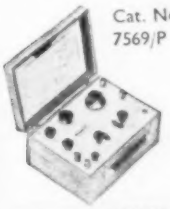

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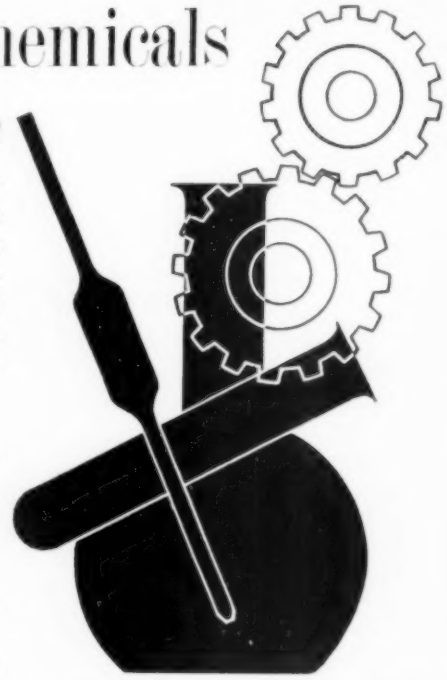

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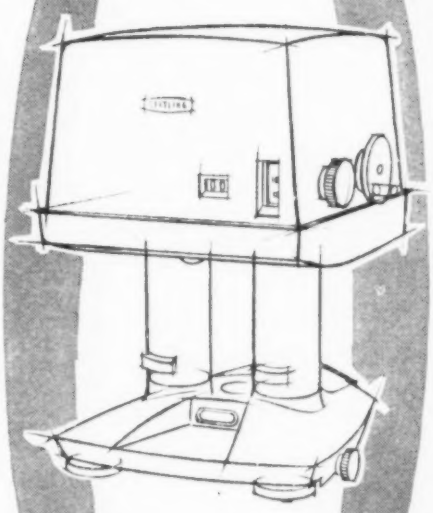

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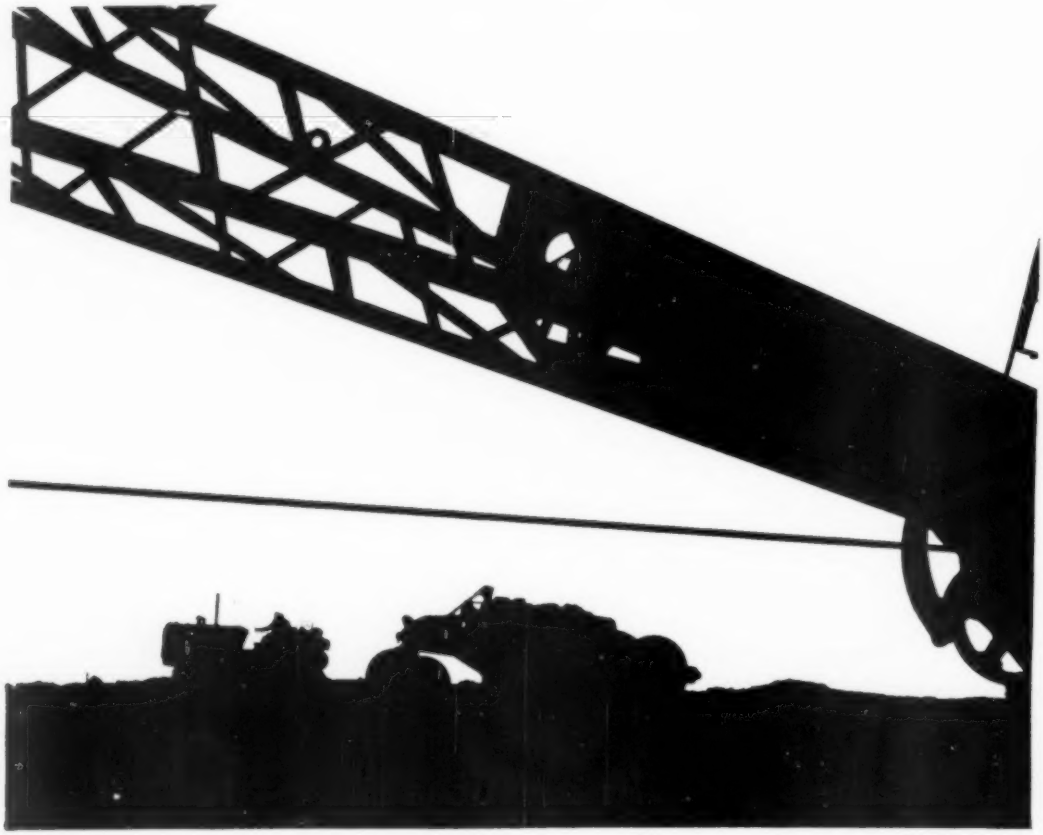

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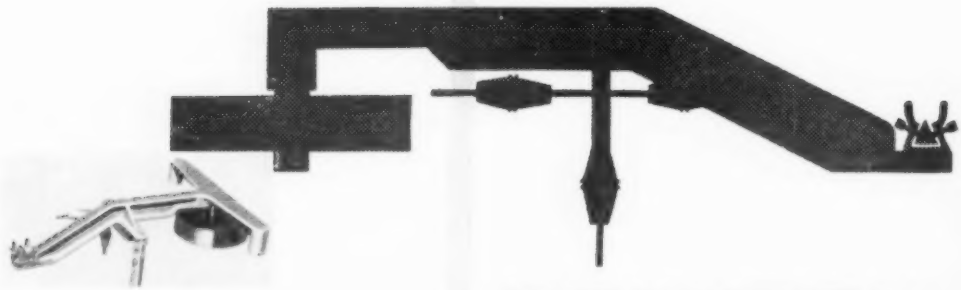

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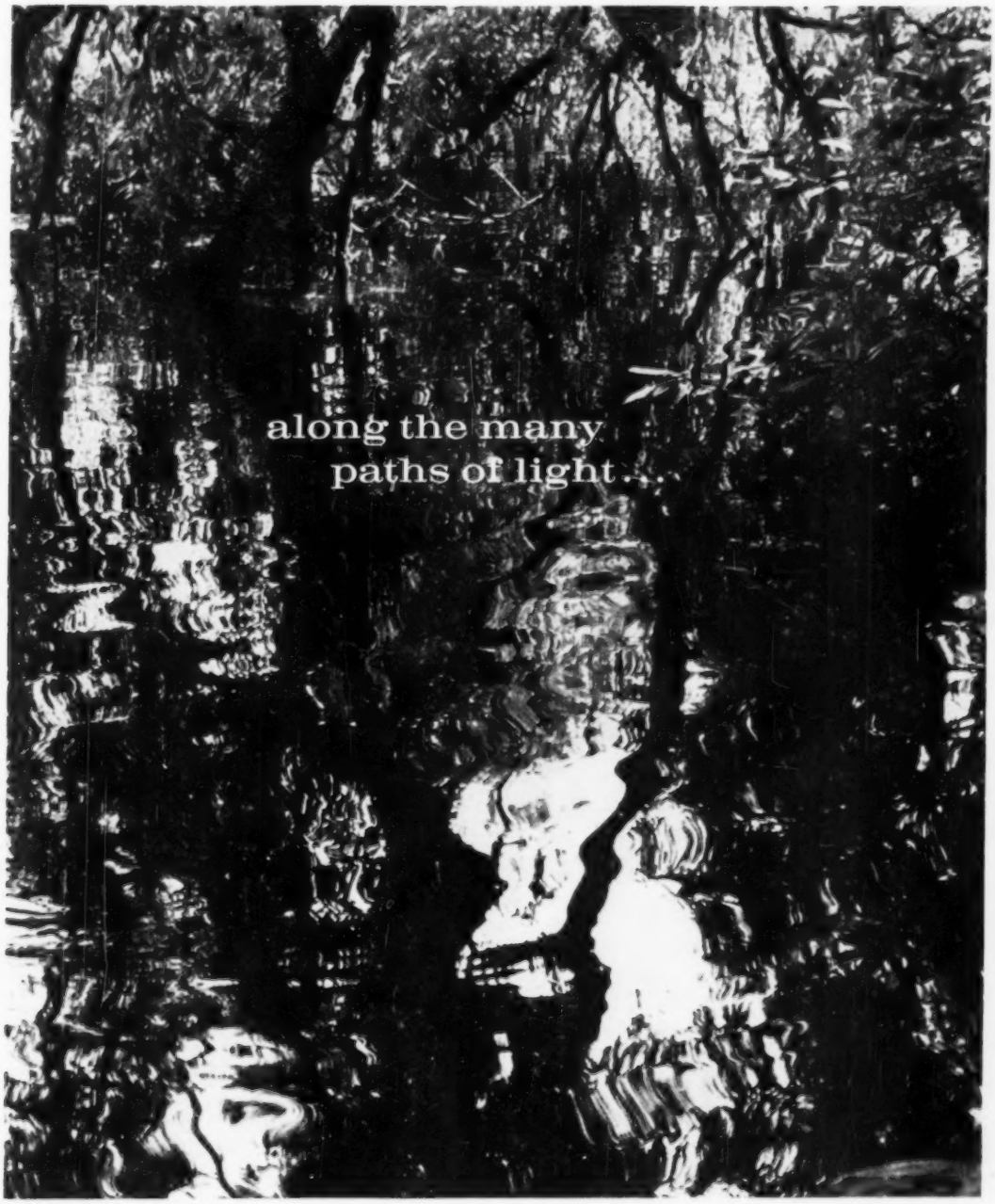

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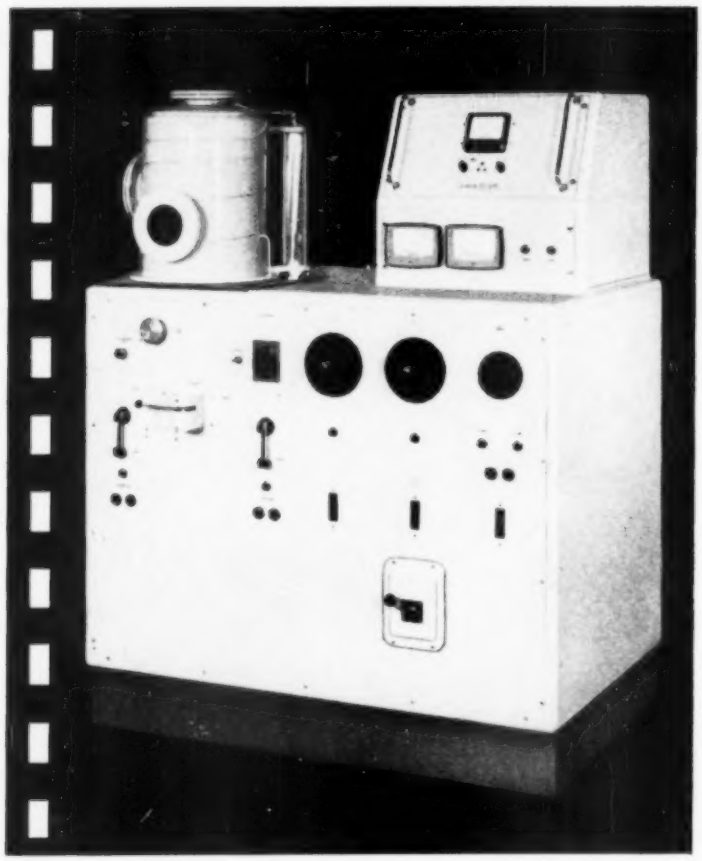

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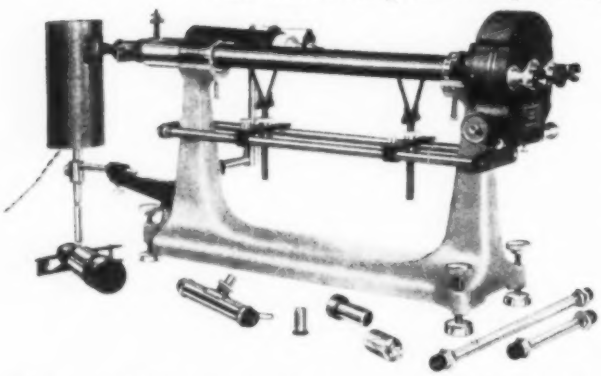

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BROADCASTING AND TELEVISION IN EDUCATION

THE presidential address entitled "Science Broadcasting in Sound and Television" delivered by Mr. A. B. Oldfield Davies to the Assembly of Corresponding Societies at the Cardiff meeting of the British Association was certainly realistic, if not also somewhat pessimistic, as to the contribution of television or sound broadcasting to the effective diffusion of real scientific knowledge. Sound broadcasting, he thought, with its greater flexibility and variety of programme services, has some substantial advantages at present over television; but he seemed very doubtful whether even the most outstanding programmes do any more than help to create an atmosphere of respect for knowledge as something good in itself. That opinion is not lightly to be dismissed and is one to be kept in mind when the expansion of educational broadcasting is being so widely discussed. The British Broadcasting Corporation is, of course, placing on a permanent basis its school television service and doubling its output; it is also continuing its school broadcasting in sound, and also the Network Three service for programmes devoted specifically to the aims of further education. The development of transistor receivers, cheap and easy to run, has in recent years opened up immense possibilities for expanding the audiences for medium-wave transmissions in the less-developed areas, particularly in Asia and Africa, though in many parts of the world short-wave broadcasting is still the main means of communication.

These new possibilities were duly noted by the Ashby Commission on Post-School Certificate and Higher Education in Nigeria. Its report, "Investment in Education"*, contains a note on new educational techniques in which they are briefly discussed. Although it is recognized that teaching through television is in its infancy and much has yet to be learned in both the use and improvement of the medium, it is recommended that, while it is still problematic when Nigeria will be able to embark on television on a large scale, channels for educational television should be reserved now, in order to ensure that, when educational television becomes practicable, the opportunity will not have been lost because the channels have been appropriated for commercial television. This, of course, is a large part of the case for allotting a second channel to the British Broadcasting Corporation, as is emphasized in the Corporation's recent annual report† and in the important speech on the future of broadcasting in Britain which the director-general, Mr. H. C. Greene, delivered to the Manchester Luncheon Club on November 9 and which has since been substantially reproduced in *The Listener* (64, 875; 1960).

Other recommendations on the new educational techniques made by the Ashby Commission include experiments with the use of the record player and magnetic tape recordings in language teaching; the organization and maintenance of a central film library for distributing to schools on a loan basis; a determined effort to use radio for English broadcasts in primary schools for at least five grades; and establishment by the Federal Minister of Education of a committee to study advances in these fields and to make recommendations for experiments in Nigerian schools. These recommendations were in fact duly noted by Lord Newton in replying for the Government on an important debate on modern aids in education in the House of Lords on November 29; and it is obviously desirable that the significance and potentialities of all such developments should receive full consideration by the Pilkington Committee on the Future of Sound and Television Broadcasting, which already has before it conflicting views as to the allocation of a third television channel. Meanwhile, it should be noted that the Minister of Education, Sir David Eccles, in opening the annual conference of the National Institute of Adult Education at Swansea, suggested the screening of television programmes of adult education. The Organization for European Economic Co-operation has already advocated the use of school television broadcasts as a contribution towards overcoming difficulties arising out of the shortage of science teachers, and, although the debate in the House of Lords brought out some misgivings on the part of school teachers, it is clear that there is wide opportunity for experiment and indeed research into the use of both sound and television broadcasting for educational purposes. Indeed, a report published last May by the University of Leeds advocated entrusting any third television channel to a Universities Television Corporation rather than to the British Broadcasting Corporation or to the Independent Television Authority.

Such a network, it was suggested, should be dedicated to education and the dissemination of knowledge, speculation and the arts, and the suggestion arose out of an examination of teaching methods. It was intended to make lectures by leading specialists available to large numbers of students at the same time, and the proposal was also concerned with the maintenance of the closest possible link between a university and its town or region. Calling for the exploitation, not the resistance, of television, it visualized spreading far more widely the activities and influence of the extra-mural departments of the university. Also the network would have at its disposal the best academic minds of the country. It would be able to provide a series of

* Investment in Education: The Report of the Commission on Post-School Certificate and Higher Education in Nigeria. Pp. v + 140. (Lagos: Federal Government Printer; London: Crown Agents for Overseas Governments and Administrations, 1960.) 5*s.* net.

† Annual Report and Accounts of the British Broadcasting Corporation, 1959–60. Pp. 175 + 8 plates. (Cmnd. 1174.) (London: H.M. Stationery Office, 1960.) 9*s.* net.

courses directed at different levels of intelligence, but possessing more depth than those now attempted; and the proposal also contemplates facilitating contact of the universities with secondary school children through its television programmes instead of merely through examinations.

This project was briefly noticed in the debate in the House of Lords, but not in Mr. Greene's speech in Manchester on November 9. Apart from a strong plea for public service broadcasting in the sense in which it had been defined by Sir Ian Jacob—as a compound of a system of control, an attitude of mind and an aim which, if successfully achieved, resulted in a service which could not be given by any other means—Mr. Greene was concerned more especially with local broadcasting and the possibility of serving minority interests, which, in a particular and limited sense, a university television network might also be said to do. He quoted Sir Ian Jacob's conception of the system of control, as full independence, or the maximum degree of independence that Parliament would accord; of the attitude of mind as an intelligent one capable of attracting to the service the highest quality of character and intellect; and the aim to give the best and most comprehensive service of broadcasting to the public that is possible. He then stressed the vital factor of the underlying motive, which must not be vitiated by political and commercial considerations. The support which was given to Lord James of Rusholme's remark in the House of Lords debate in reference to the peak viewing hours, that we have sold our broadcasting system to advertising, indicates how much agreement there is here with Mr. Greene's argument.

Mr. Greene sought to show how, precisely because of this situation with regard to the peak hours, only a public service system could ensure for the local audience a genuinely local and independent programme. In support of the British Broadcasting Corporation's claim, he adduced its experience in resisting political and commercial pressures, which could be intense at the local level, in collaborating with universities, technical colleges and schools in providing educational programmes, and in the impartial reflexion of all kinds of controversies. He also mentioned the support of the Corporation's nationally based service in collecting items for the local audience and the existence of its three national networks as sources of programmes at times when the local station is not putting out its own programmes. He is convinced that there is plenty of good material for local broadcasting and that such broadcasting has an essential contribution to make to the life of the community, though he maintained that this can only be made within the framework of public service broadcasting, and doubted whether a universities television network could prove effective enough to resist pressure or be efficient enough in making use of the channels available.

Mr. Greene was concerned rather with low-powered transmitters operating over a radius of no more than four or five miles; in such a network of local stations, sound radio could well provide a service beyond the reach of television and tap the neglected wealth of resources in the universities and elsewhere as well as assist in promoting a more vigorous local culture. Mr. Greene has been criticized for his omission of any reference to religious broadcasting in this connexion, and there is clearly something to be said for any local VHF stations including local councils of churches with other local institutions with which they can work in harmony while maintaining standards of broadcasting. Apart from this, the fact that a Cambridge firm of television and radio equipment manufacturers has already outlined a scheme for establishing a hundred local VHF radio stations in Britain, run, not as part of a big organization, but by individual owners as local affairs, and with the transmitter available to the education authorities for schools broadcasting during the day when it is not in use for the main transmission, confirms that local sound broadcasting is already practicable. Apart from the scheme outlined in this pamphlet issued by Pye, Ltd., about a hundred companies have in fact been registered with the object of running such local stations if and when it becomes possible.

In opening the debate in the House of Lords, Lord Bessborough suggested that the very success of sound radio in education is one potent reason why no more than 2,500 out of some 30,000 schools in Britain take the educational television programmes of the British Broadcasting Corporation and of Associated Rediffusion. He agreed with Mr. R. Hickman, of the National Union of Teachers, that many more programmes are needed, but that it is essential to ensure the utmost co-ordination and co-operation among initiating companies, who must build up and maintain units able both to become expert in teaching methods and techniques, and also to maintain the closest possible contact with schools. Lord Bessborough urged also that full advantage should be taken of special opportunities in universities, and particularly that universities should be enabled to start pilot schemes; and although Lord Newton took up this point in his reply, he suggested that the initiative should come mainly from the universities themselves, and that the Pilkington Committee might express opinions on the merits of university broadcasting and television.

Much the weightiest speech in the debate was that of Lord James of Rusholme. He acknowledged the very great contribution which television—and still more sound broadcasting—has made to education in Britain, and paid tribute to the work of the British Broadcasting Corporation, particularly in research and development, and to that of the Schools Broadcasting Council, through which the Corporation has worked. There is still need, Lord James thought, for much research in the use of broadcasting, and we might be on the threshold of fundamental developments. There are also the limitations imposed by finance, and he strongly supported not only the plea put forward by the Corporation in its current report for the retention of the whole of the licence fee but

also increasing the fee to an economic figure. The effective use of television, however, depends ultimately on the imagination and skill of the class-room teacher, and he thought it futile to over-emphasize the value of television in the schools when these programmes have to contend with the 'diseducation' effect of those broadcast at the peak hours for child-viewers—between 6 and 9 p.m.

Other speakers in the debate, like Lord Aberdare, Lord Strang and the Baroness Swanborough, stressed the importance of research and of the influence of the teachers, which, it was emphasized, are not replaced either by sound or by television programmes, and Lord Newton readily responded. There is no question, he said, of attempting to meet the present shortage of teachers by trying to use broadcasts as a substitute for teachers, and he suggested that the main function of broadcasting in Britain, both on sound and on television, is enrichment of teaching, as opposed to the direct teaching method of the kind used in the United States. As Lord Newton understood it, this meant that broadcasts could reinforce a teacher, extend the range of teaching and provide fresh help in the classroom, and he thought that among teachers there is much serious thought and goodwill and the recognition that this new medium is something to be taken seriously and of great potential importance. Speaking about equipment, he merely observed that the Minister of Education has no direct financial control over the purchase of equipment for the purpose; this is entirely a matter for the local education authorities. He agreed as to the need for more research, but referred to the work of the National Committee for Visual Aids in Education, and stated that the report of the Organization for European Economic Co-operation, "Teaching through Television", is being studied by the Minister of Education. It is the policy of the Colonial Office to encourage development of sound and television broadcasting on local lines and with the use of local talent. Sympathetic consideration is also being given to financial aid for a further period to the Overseas Visual Aids Centre in Tavistock Square.

Lord Newton's hope that this debate would stimulate constructive thought in educational circles about the possibilities of school broadcasts and television should certainly be fulfilled, and his view that the great trusts and foundations could give a most useful lead in research in this field should be duly noted. Lord Newton thought, too, that the teachers' attitude would be a main determining factor, and that this might be particularly influenced by the results of research. As yet, however, as was almost universally acknowledged in the debate, sound broadcasting is by far the more important, and a prime task accordingly is to see that the resources and techniques available are adequate and appropriate. Nevertheless, although the British Broadcasting Corporation's views on local broadcasting, as set forth both by the Director-General himself and in the Corporation's current annual report, embrace full and free association and co-operation with universities, local authorities, newspapers and other important institutions within the local communities, there is an influential volume of opinion, not reflected in the debate in the House of Lords, which is strongly opposed to any extension of the British Broadcasting Corporation's power in this field. That the British Broadcasting Corporation is seriously misrepresented in this connexion may be of relatively little importance: some of the misrepresentations have been decisively refuted by Mr. Greene. It is more serious, however, that the picture of local broadcasting in other countries should also be distorted in this same connexion, and more debates, free from party political bias and commercial misrepresentation, are undoubtedly needed if a sound judgment is to be reached as to the manner in which educational broadcasting, whether in sound or television, should be approached. Further consideration is required of the way in which the universities and schools might co-operate, and how in the development of local broadcasting and television the conception of public service could best be preserved and to ensure that there is no sacrifice of the public interest—educational or cultural—to sectional or purely financial advantage.

THE CORRESPONDENCE OF ISAAC NEWTON

The Correspondence of Isaac Newton, Vol. 2
1676–1687. Edited by Prof. H. W. Turnbull. Pp. xiii + 552 + 6 plates. (Cambridge: At the University Press, 1960. Published for the Royal Society.) 147*s.* net.

THE decade (1676–87) spanned by the present volume was an eventful one in Newton's life. While he was harassed by a rather nasty controversy with the Liège Jesuits about the theory of colours, he had to face, in friendly rivalry, Leibniz's first claim to the independent discovery of the infinitesimal calculus (1676–78). Then (1679–80) came the fateful discussion with Hooke about the fall of a body to the centre of the Earth, which led Newton's thoughts to the more general problem of finding the trajectory of a gravitating body. He soon received a further incentive to pursue this line of investigation from Flamsteed's controversial interpretation of comet observations at the end of the year 1680 (Old Style). Finally, prompted by Halley's famous visit in 1684, he was induced to write down his decisive results and to elaborate them during the ensuing years (1684–87) in the form of the *Principia*.

This succession of dramatic incidents fills the pages of this fascinating volume, in which are assembled not only the well-known documents which form the basis of existing biographies but also a large number of hitherto unpublished letters and manuscripts which throw much new light on the events and on Newton's complex personality. The very excellence of the editor's work elicits in but one respect an expression of regret: one would wish that he had been somewhat more generous in the inclusion of auxiliary documents not strictly of epistolary character; for example, from the important accounts of the work done in Great Britain on infinite series, drawn up by Collins for the information of Leibniz, we are only given those passages which refer directly to Newton; this documentation,

however, is too fragmentary to be of any use to the serious student, and one may question very much the wisdom of such an effort at economy. It is true that these documents, as well as others equally essential, like the treatise *De Motu*, exist in print; but the books in which they are published have practically vanished from the market and are even not common in public libraries; a reprint in the context of the *Correspondence*, which would not have sensibly increased the bulk of the volume, would therefore have been most welcome. Perhaps an earnest plea for a somewhat broader conception of the selection of material may still have some influence on the preparation of future volumes.

One hitherto quite unknown episode, revealed by the present publication, is the prolongation of the futile controversy about Newton's theory of colours started by the English Jesuits of Liège: one assumed that it was closed by the last answer from Newton published in the *Philosophical Transactions* in 1676 (Letter 173 in this volume), but we now learn that the exchange of letters between the Jesuit Lucas and Newton went on at intervals during two more years, the former becoming more and more venomous and the latter increasingly rude. Obviously, the mixture of cunning casuistics and pedantic irrelevancy displayed by his opponent was too much for Newton's robust common sense and sound logic, but he had also a deeper motive for so insistently pursuing a pointless and sordid quarrel: Lucas had found for the elongation of the solar spectrum a smaller value than Newton, and this sufficed to rouse the morbid suspiciousness which the latter manifested whenever he thought his accuracy and veracity impugned. Lucas's attempts at belittling the discrepancy only increased Newton's exasperation, and unfortunately made him blind to the true explanation—the difference in dispersive power of the glasses, although this was actually suggested (Letter 200) (amid a number of irrelevances) by Lucas himself! Hooke (Letter 223) wondered at Newton's "patience"—unaware of this tragi-comic aspect of the situation.

At the same time, through the intermediary of Oldenburg, a thorough confrontation was taking place of the respective achievements of Newton and Leibniz and their respective followers in the treatment of various algebraical and geometrical problems by a method of series expansion, involving a limiting process of derivation or differentiation as well as the inverse process of integration. To this correspondence Newton contributed, somewhat reluctantly, two remarkable Letters (165 and 188), of which especially the second ("epistola posterior") is a document of capital interest, retracing as it does in great detail the successive steps through which Newton arrived at the full realization of his method. The whole material pertaining to this momentous development (unfortunately with some curtailment, as mentioned above) is here fully elucidated by the editor's especially careful and elaborate annotation.

We then pass to the no less remarkable circumstances which led to the genesis of the *Principia*. The first act is well known already by the accounts given by Rigaud and Rouse Ball, and, quite recently, by J. Lohne in *Centaurus* (vol. 7, pp. 6–52; 1960). Challenged by Hooke's acute criticism, Newton is forced to rectify his views concerning the path by which a falling body would eventually reach the centre of the Earth; and from this academic problem he is further led (as we know from the later correspondence with Halley) to study the dynamical behaviour of bodies acted on by gravitation. It appears that the crux of this problem was neither the formulation of the inverse square law (which had been inferred from Kepler's laws by Hooke, Halley and Wren as well as by Newton), nor the conception (inspired by Galilei's treatment of projectiles) of the planetary motion as a uniform rectilinear one modified by an attraction from the Sun; the difficulty was to determine the shape of the resulting trajectory. This was the decisive step which Newton then (1680) took; but, as usual, after solving the problem, he "threw the calculation by, being upon other studies".

It was not long, however, before his attention was again turned to the same question, this time by a concrete case of astronomical observation. In the last months of the year 1680 (Old Style) two comets had been successively observed, the first moving towards the Sun, the second away from it. Flamsteed, who had himself contributed to these observations, suggested that the two objects were the same comet, first attracted, then repelled by some magnetic action of the Sun; and he solicited Newton's opinion. The ensuing correspondence is now for the first time published in full, and it enables us to form a picture of this incident rather different from the somewhat misleading account of it given by Brewster. Flamsteed's magnetic theory, as one imagines, did not resist Newton's remarkably sound criticism, based on the empirical knowledge of magnetic phenomena; but at the same time, Newton accurately described the orbit which a single comet could have followed under the action of gravity: at first, he hesitated to accept the proposed identification of the two objects on the ground that there was no precedent for such a form of cometary orbit, all the known ones being practically rectilinear. However, as better observations became available, it became clear that they did fit a single orbit of the type indicated by Newton.

It is not surprising, therefore, that when Halley, in August 1684, asked him what would be the trajectory of a gravitating body under the inverse square law, Newton had the answer ready. (Lohne's surmise, expressed in the aforementioned article, that Newton did not then have the proof, but only worked it out after Halley's visit, is not in harmony with Newton's own declaration, nor with other circumstantial evidence.) The story of how Halley succeeded in persuading Newton to write the *Principia*, how Hooke's not unjustified reclamation of priority nearly wrecked the enterprise, how Halley's tact and devotion rescued it and carried it to a good ending, is too well known to need repetition. But it is a delight to read it again, in the protagonists' own words, so faithfully recorded and beautifully printed.

L. ROSENFELD

ATOMS AND MOLECULES

Basic Physics of Atoms and Molecules

By Dr. U. Fano and L. Fano. Pp. xv+414. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1959.) 80s. net.

THE book is divided into two parts and ten appendixes. The first part presents the basic facts concerning the structure of matter and introduces the new concepts required to correlate them. The

second part deals with aggregates of particles, being chiefly concerned with chemical bonding. Mathematical background is provided in the appendixes.

At an early stage most text-books introduce experimental evidence concerning the wave aspects of particle beams, and, from a comparison with beams of light, the Schroedinger wave-equation quickly follows. This book arouses interest because the authors prefer to discuss the analogy between polarization of light beams and of molecular beams. They consider that discussion of a system having a small number of eigen-states is more instructive, and, in addition, polarization in the classical treatment of radiation has much in common with ideas of quantum mechanics. The analogy brings out clearly the principle of superposition, but their picture is somewhat clouded by a premature introduction of rotational matrices, the mathematics of which has fortunately been relegated to an appendix.

The second part will appeal more to the chemist than the physicist, who would prefer an account of metals and semi-conductors and a more detailed description of the simple molecules. Indeed, the chemist may find the whole of this part too brief and qualitative.

Finally, it is difficult to decide for whom the book is intended. The authors state in their preface that it is directed primarily to research workers in the natural sciences (and undergraduates) and presupposes only a general knowledge of physics and mathematics. This view is supported when, in two footnotes, they find it necessary to explain what is meant by the exponential function, and in the first few appendixes when among other subjects they describe the relative motion of two particles and introduce the concept of complex numbers. The next appendix gives the geometrical calculation of rotational matrices and is followed by an equally difficult one on the mathematical formulation of quantum laws. A mathematical derivation of the Uncertainty Principle is given, whereas the qualitative treatment involving the 'gamma-ray microscope' may have been more consistent with the aims of the preface.

On the whole, the average student will find this book particularly heavy going. G. A. JONES

RACIAL PREJUDICE AND MENTAL HEALTH

Race Relations and Mental Health

By Marie Jahoda. Pp. 48. (Paris: Unesco; London: H. M. Stationery Office, 1960.) 1.75 NF.; 2*s*. 6*d*.; 0.50 dollars.

THE virulence with which racial prejudice has made its appearance in the present century is one of the strangest and most disturbing phenomena of present times. Race hatred and conflict thrive on scientifically false ideas and are encouraged by ignorance. To illuminate errors in fact and reasoning and to make known conclusions reached in various branches of science and to combat racial propaganda, the Director-General of Unesco was asked to study and collect scientific material concerning questions of race; to give wide diffusion to the scientific information collected; and to prepare an educational campaign based on this information.

Before this programme could be carried out, it was necessary for Unesco to have the relevant facts at its disposal. Accordingly, a number of prominent scientists were asked to summarize the main results in the field of their specialization. Some of them have already presented the results of their investigations in booklet form, and, now, Marie Jahoda examines in *Race Relations and Mental Health* the psychogenetic bases of prejudice and the relationship between prejudice and mental health. The work is commendable for the objective way in which it is presented and, where the author presents her own views, makes it clear that they represent her opinions.

Whether racial antagonism is based on fact or fancy becomes a question of the adequacy of inference; there is a growing body of empirical evidence to show that inadequate reality-testing is characteristic of many who feel hostile to racial outgroups. This is well brought out by Jahoda who shows that the same qualities which are given as reasons for disliking another racial group are often highly appreciated when found in a member of a favoured group. Another cause of prejudice is that the human propensity to make generalizations and prejudgments often results in some economy of mental effort. Such pre-judgments can harden into rigidly stereotyped thinking which eschews reality-testing even when facts are available.

After a psycho-analytical study of the deeper causes of prejudice, Jahoda discusses whether or not prejudice is inevitable. Here she refuses to be spuriously optimistic. Racial antagonism, according to her psycho-analytically oriented interpretation, is a deeply meaningful support to the individual of low mental health. The psychological need which leads to racial antagonism is universal and will continue to exist during the foreseeable future. Few will disagree with this conclusion or with her personal belief that "to deprive one's sense of identity from work or from stamp collecting or from mountain climbing may be psychologically as precarious as to deprive it from prejudice against underprivileged groups; but it may help one to live without hating either oneself or one's neighbours".

T. H. HAWKINS

CHRISTIANITY AND SCIENTIFIC PROGRESS

Science, Technology and the Christian

By Prof. C. A. Coulson. (The Beckly Social Service Lecture, 1960.) Pp. 111. (London: The Epworth Press, 1960.) 8*s*. 6*d*. net.

PROF. COULSON'S Beckly Social Service Lecture is addressed primarily to those who share his Christian faith, for, in accordance with the purpose for which the Lecture was instituted, he seeks to show why the Christian, as such, should be concerned with technology as well as with science, the nature of the issues that are involved, and the manner in which Christians could contribute to the solution of some of the problems that arise, for example, in the control of nuclear power, the application of automation, or in food and population policies. With Archbishop William Temple, he regards Christianity as the most materialistic of religions, and in the same sense. Much in this Lecture

accordingly should be welcomed by the scientist or technologist who shares that sense of the ethical values which Smuts and others since, like Hinshelwood, Appleton and Ashby, have expounded, whether or not Prof. Coulson's own faith is fully accepted. This attempt to stir Christian people to constructive thinking and the facing of change leads, for example, to an eloquent plea for an educational system which allows no child to pass through it without some acquaintance with both science and technology.

In a way, the Lecture could be described as an attempt to interpret in a specific Christian context the essential message of the Duke of Edinburgh's Study Conference at Oxford in 1956. The challenge of change is presented just as clearly, and Prof. Coulson brings out the social and human issues involved, to the solution of which he is convinced that Christian principles of conduct have an essential contribution to make. Here, however, the emphasis on the pace of change and the decay of tradition recalls a fine passage in A. N. Whitehead's *Adventures of Ideas*, which discusses routine, tradition and change and their implications in the modern world.

Prof. Coulson is never trivial and writes with a sincerity, dignity and restraint that should enlist the support even of those inclined to take umbrage at his claim that some of his principles are specifically Christian, in the immense task to which he calls us of seeking to use creatively and imaginatively all the vast powers now at the disposal of mankind, with the sensitive insight into human needs, the profound respect for human personality and the confidence that the world has learned particularly from the life of Christ. Prof. Coulson's scholarship and wide reading characterize this short book as profoundly as his human sympathy and his Christian faith, and although it is unfair to expect too much in such matters of a published lecture, regret may be entertained that the book loses something of its full value as a stimulus to further study through the absence of an index and all but a handful of references.

R. Brightman

FROM ARTS AND CRAFTS TO TECHNOLOGY

A Short History of Technology from the Earliest Times to A.D. 1900

By T. K. Derry and Trevor I. Williams. Pp. xviii + 782. (Oxford: Clarendon Press; London: Oxford University Press, 1960.) 38s. net.

As the large five-volume *History of Technology* was being written by Prof. Charles Singer and his colleagues, an abridged edition was planned to meet both the needs of a wider readership (the larger handbook unfortunately being beyond the means of the average reader) and the desirability of establishing more firmly in the minds of both historians and engineers the relation between the history of technology and history in general. Imperial Chemical Industries have again generously supported this venture. The fortunate fact that one of the authors, Dr. Trevor I. Williams, is not only well known as the editor of *Endeavour* but was also for several years engaged in assisting Prof. Singer in producing his pioneer handbook has made it possible to use the evidence and manuscripts collected in compiling the five-volume work. This is also the source of most of the 353 figures used in the text of this new book.

However, the authors have by no means produced merely an abridgment of Singer's handbook. They have planned their own "technological history and history of technology", in which the essential trends and developments are presented in a concise and very readable form. A good bibliography, designed for the English reader, points the way for further detailed work on the subjects broached in the various chapters.

The book consists of two sections, each of which is preceded by a "General Historical Survey" of the period covered. The first section "From the Earliest Times to A.D. 1750" takes up about one-third of this 700-page text-book. In nine thirty-page chapters we are introduced to the crafts necessary for producing food and satisfying other domestic needs, mining and metallurgy, transport, recording and communications, sources of power and the earliest forms of the chemical industry, and their history is carried up to the Industrial Revolution.

The remaining two-thirds of the book and more than 220 illustrations cover "The Industrial Revolution to A.D. 1900". This upper limit has been quite rightly chosen by the authors, as "by 1900 the most advanced societies were beginning to register a change in the aims, as distinct from the methods, of technology. For man was no longer pitting his wits against Nature merely for the easier satisfaction of long-felt wants. . . . With the entry upon a new period, in which necessity ceases to be the mother of invention", the inventor began to create new wants, and technology is embedded firmer than ever in the general history of civilization.

The last section deals with many tools, methods and machines, with which most of us are still familiar, even if some forms of technology are now slowly disappearing. Here we are confronted with the history of the steam engine and turbines, machine tools and the development of interchangeable machine parts. New materials such as wrought and cast iron, steel and concrete begin to play a prominent part. Transport is transformed by the coming of the steamer, railways, bicycles, motor-cars and aeroplanes. Coal-mining grows and fosters the cheap production of iron and steel and initiates the coal-gas and coal-tar industries. Pure synthetic chemicals such as soda, sulphuric acid, nitric acid and ammonia are basic products for a new chemical industry. Rubber and petroleum create the 'motor age', and there is the new electrical industry which provides better communications, lighting and power. Finally, there is modern mechanized farming and the processing and preservation of farm-products by canning and refrigeration.

These and many more subjects are here presented in a form which will prove to be most valuable to the historian without technical training, who, in his turn, will be confronted with the gaps in our knowledge for which he will be called on to provide the clues for further research, together with the engineer and the technologist. Seven tables relating political and economic historical data to those of technology are given at the end of this book, which is without doubt a most valuable introductory manual to a historical discipline still in its pioneering age.

R. J. Forbes

Algebraic Curves

By Prof. J. G. Semple and G. T. Kneebone. Pp. xiii + 361. (Oxford: Clarendon Press; London: Oxford University Press, 1959.) 45*s*. net.

RECENT work on algebraic geometry has been much concerned with placing the subject on foundations which should be genuinely algebraic; a programme set on foot by van der Waerden some twenty-five years ago. The theory of algebraic curves is a very important section of algebraic geometry, and while R. J. Walker's excellent treatise, based on methods of modern algebra, has been available for ten years, an account on similar lines, but tailored to suit the student in his final undergraduate or first postgraduate year, has been needed. This need has now been fully met. Semple and Kneebone start from the beginnings, and take the general theory as far as the Riemann–Roch theorem; the exposition is always clear and precise, and each chapter begins with a survey of what is to be found therein and concludes with valuable exercises and notes. No very extensive algebraic equipment is required in the early stages, and to make the work self-contained an appendix summarizes practically all the needed work on rings, fields, polynomials and elimination theory. Two chapters initiate special studies: that on "Coordinates of a Curve" is a most helpful introduction to the Cayley form for algebraic varieties, while that on "Local Geometry in S_2" deals with a logical algebraic basis for what used to be called 'indefinitely near points'. It should be added that references to the older methods involving algebraic functions and Riemann surfaces are not absolutely excluded. An older generation might ask what Salmon would have made of all this, but, remembering that according to his contemporaries Salmon was "never a calculus man", perhaps he would have come to appreciate this new close convolution of geometry with algebra.

T. A. A. BROADBENT

Chemical Analysis of Resin-based Coating Materials

Edited by C. P. A. Kappelmeier. Pp. xxvii + 630. (New York: Interscience Publishers Inc.; London: Interscience Publishers, Ltd., 1959.) 147*s*.

THIS collection of papers on the analysis of coating compositions was edited by an expert in this particular field, the late Dr. C. P. A. Kappelmeier, who studied under Baeyer and Wieland.

The book contains practical contributions from twenty-six senior chemists of many leading chemical firms situated in all parts of the world. It constitutes a unique and welcome compilation of tested classical and modern methods for the analysis of resins, plastics, paints, solvents, etc.

C. Schwarzenback and W. Schneider present an excellent chapter on the complexometric analyses of metallic additives: A. Z. Conner describes the techniques of paper and columnar chromatography, but gas-liquid chromatography receives only brief mention. Infra-red and ultra-violet absorption methods receive detailed treatment, and even the applications of mass spectrometry are succinctly discussed in the 'rosin' section.

Specialized chapters are devoted to alkyd and synthetic thermoplastic resins, latex paints, cellulose lacquers, drying oils, etc., and much helpful laboratory detail is provided. This volume will undoubtedly prove a most valuable reference work for industrial analysts who are concerned with the quantitative and qualitative examination of the wide range of coating compositions now being manufactured by the chemical industries. It is, unfortunately, rather highly priced for a book of 630 pages, but it is most legible and printed on excellent paper.

D. T. LEWIS

Microbiology

Historical Contributions from 1776 to 1908 by Spallanzani, Schwann, Pasteur, Cohn, Tyndall, Koch, Lister, Schloesing, Burrill, Ehrlich, Winogradsky, Warington, Beijerinck, Smith, Orla-Jensen. Edited by Raymond N. Doetsch. Pp. xii + 233. (New Brunswick, N.J.: Rutgers University Press, 1960.) 5 dollars.

THIS book follows a commendable trend in American scientific publishing during recent years of presenting, in abridged form, excerpts from the works of the great scientists of the past. For those of us—the majority—who will never have an opportunity of reading many of the original papers, such syntheses provide an admirable substitute. As the editor wisely points out, the selection of papers is necessarily arbitrary, and there is bound to be difference of opinion regarding inclusions and omissions. Nevertheless, few will quarrel with the majority of the works included here, each of which is prefaced with a brief biographical introduction and a picture of the author.

The collection will be of value to anyone interested in the history of science, and would be a useful adjunct to any course covering this period of scientific history. It should prove particularly valuable in schools where the historical aspects of scientific discovery tend to be overlooked. The diversity of subjects covered provides a fascinating insight into the manifold applications of the so-called scientific method.

W. H. DOWDESWELL

Transactions of the International Astronomical Union

Vol. 10: Tenth General Assembly held at Moscow, 12–20 August, 1958. Edited by D. H. Sadler. (International Council of Scientific Unions: International Astronomical Union.) Pp. ix + 774. (Cambridge: At the University Press, 1960.) 90*s*. net.

THIS volume contains the Proceedings of the meeting of the International Astronomical Union held in Moscow (1958). It contains the resolutions adopted at that meeting and the reports and proceedings of the various Commissions within the Union. The reports of the Commissions provide valuable summaries of the state of the subject and provide extensive bibliographies of original research done, in the preceding three years, in those fields which come within the scope of the Commissions. Four joint discussions (solar flares and corpuscular streams, nucleogenesis in stars, the luminosity of cepheids and astronomical observations with artificial satellites, rockets and balloons) which took place during the meeting are reported. A list of members of the Union and their addresses, correct to October 1959, together with the membership of the Commissions, is also appended.

It is noted that the General Secretary is contemplating action to expedite the publication of the *Transactions*. The rapid publication of the *Transactions* in smaller volumes would certainly enhance their usefulness as a reference work.

D. MCNALLY

EFFECT OF ALPHA- AND BETA-MELANOCYTE STIMULATING HORMONES ON THE SKIN COLOUR OF MAN

By Prof. AARON B. LERNER and Dr. JOSEPH S. McGUIRE

Section of Dermatology, Department of Medicine, Yale University School of Medicine, New Haven, Conn.

SIX years ago it was shown that intramuscular injection into man of a relatively crude alkali-treated extract from hog pituitary glands produced darkening of skin and nevi[1]. This darkening was similar to that observed in patients with adrenocortical insufficiency and some types of pituitary tumour. The pituitary fraction used at that time had a moderate amount of melanocyte stimulating hormone activity, but almost no other measurable hormonal effect. Later, two types of melanocyte stimulating hormones, α- and β-, were isolated from the pituitary glands of hogs, cows, sheep, horses, monkeys and human beings[2-5]. The structure of α-melanocyte stimulating hormone in all species is the same, although it has not been completely established for man. On carboxymethyl cellulose columns, α-melanocyte stimulating hormone from man behaves the same as that from other species[5]. On the other hand, there are at least five varieties of β-melanocyte stimulating hormone; and it appears that in some species two forms may exist (Fig. 1)[7]. Since the pituitary material used in the original experiments in man was crude and because alkali treatment prolonged the melanocyte stimulating hormone activity as tested with frog skin *in vitro*, it was desirable to repeat the experiments with pure α- and β-melanocyte stimulating hormones. In addition it was possible to refine the techniques for measuring changes in skin colour.

Traces of vasopressin in our best preparation of α-melanocyte stimulating hormone prevented us from using this material in human beings. Fortunately, we were able to use synthetic α-melanocyte stimulating hormone generously provided by Dr. Klaus Hofmann and his colleagues, who accomplished its synthesis in 1959[8]. Although the synthetic α-melanocyte stimulating hormone, unlike the naturally occurring hormone, had a formyl group on the epsilon amino-group of lysine, and glutamine in place of glutamic acid, its activity on frog skin was the same as that of the natural hormone. 100 mgm. of β-melanocyte stimulating hormone was prepared in our laboratories from hog pituitary glands by Dr. Teh Lee and Mrs. Vina Buettner-Janusch, and another 100 mgm. was supplied by Drs. R. Guillemin and A. V. Schally.

α–MSH

CH_3CO–SER·TYR·SER·MET·GLU·HIS·PHE·ARG·TRY·GLY·LYS·PRO·VAL·NH_2

β–MSH

ASP·GLU·GLY·PRO·TYR·LYS·MET·GLU·HIS·PHE·ARG·TRY·GLY·SER·PRO·PRO·LYS·ASP
↓ SER ARG ARG
ALA·GLU·LYS·LYS

Fig. 1. Structure of α- and β-melanocyte stimulating hormones showing the common sequence of amino-acids in both peptides. α-Melanocyte stimulating hormone from hogs, cows, sheep, horses and monkeys is the same. The sequence of hog β-melanocyte stimulating hormone is given, and the sites of variation in different species are shown. Thus in cows and sheep serine replaces glutamic acid; in monkeys arginine replaces lysine (refs. 5, 6); in horses arginine replaces proline (ref. 6); and in human beings the tetrapeptide Ala·Glu·Lys·Lys is added to the N-terminal aspartic acid, and arginine replaces lysine (ref. 4). In some species, for example, sheep and monkeys, both glutamyl and seryl β-melanocyte stimulating hormone are present (ref. 7)

Four Negroes took part in the work. From the early experiments we found that, within limits, the darker the individual the greater his response to melanocyte stimulating hormone. Short supplies of both α- and β-melanocyte stimulating hormones necessitated short-term experiments with darkly pigmented subjects. Throughout the experiment changes in colour of the skin were recorded with two kinds of reflectance measurements and two kinds of colour photography. Photographs before and after each experiment were taken on the same roll of film so that the problem of variability in processing the colour film would not occur. Professional 'Ektachrome *E*-3' was used. Illumination was provided by three electronic flash units, and an Eastman 81A colour correction filter was used. All exposures were f.8. Also, 16-mm. 'movies' with colour film were taken of the face for 2–5 sec. daily. Reflectance measurements of the centre of the forehead and of the back of the forearm were made with a Cary model 14 recording reflectance spectrophotometer using light of 3500–7000 Å. Measurements of the forehead, cheek and arm also were made with a Photovolt model 610 photoelectric reflexion meter without filters and with red, blue and green filters as described earlier[1]. The injections, each 1·0 ml. in volume, were administered intramuscularly into the deltoid muscle. The melanocyte stimulating hormone was first dissolved in saline and then diluted with an equal volume of 16 per cent gelatin solution. The final concentration of melanocyte stimulating hormone usually was 4·0 mgm. per ml. This preparation was used in all subjects except J. R., who received the hormone in saline alone. Three of the subjects were employed at indoor jobs during the day. The fourth (R. R.) was unemployed for the duration of the experiment. All subjects avoided exposure to sunlight so far as it was practical and wore caps and shirts with long sleeves whenever they were out of doors.

Subject 1. J. R. was a 32-year-old college student. On the first day the following results of blood studies were obtained: fasting blood sugar, 75 mgm. per cent; blood urea nitrogen, 17 mgm. per cent; carbon dioxide, 26·7 m.equiv./l.; chloride, 107 m.equiv./l.;

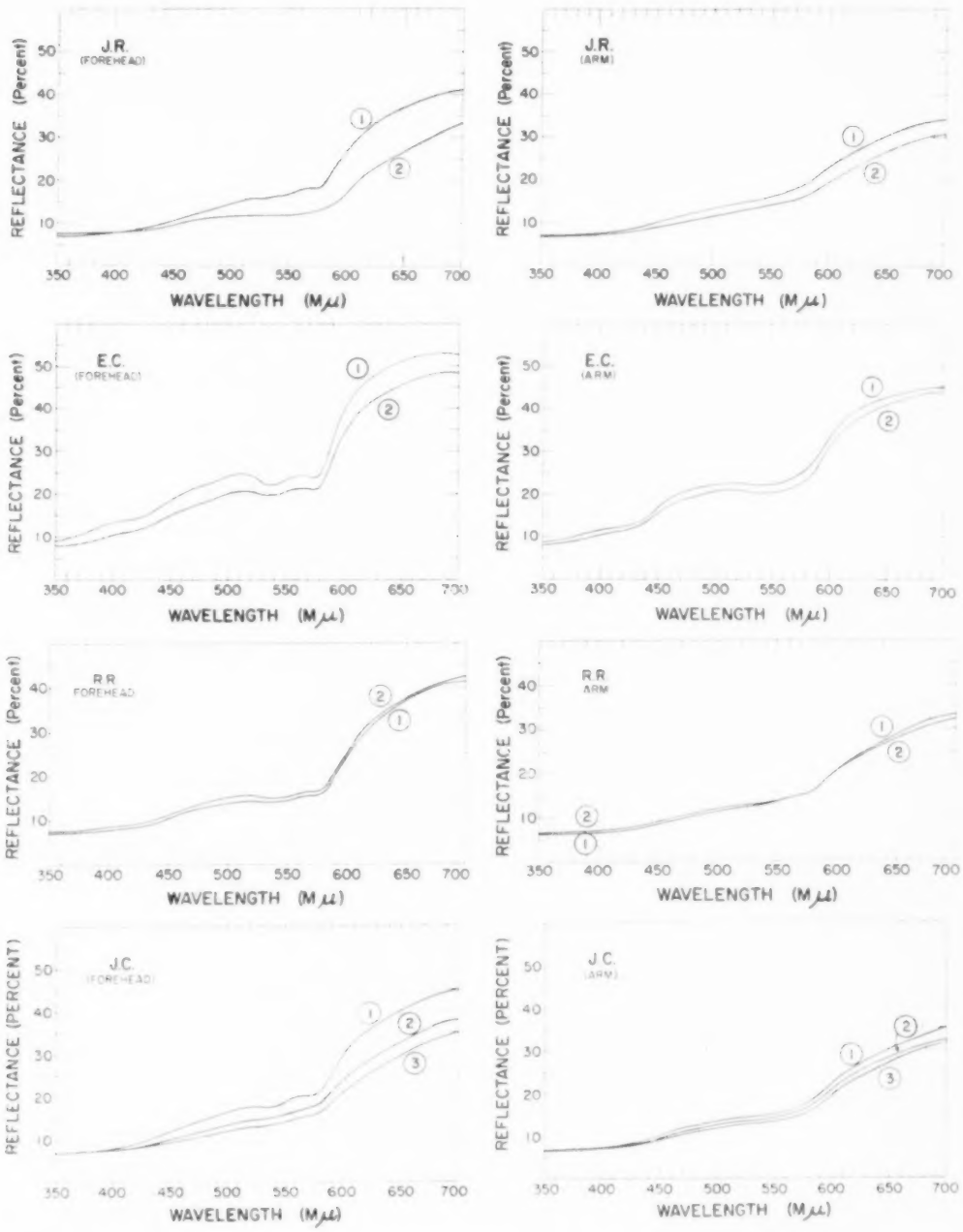


Fig. 2. Effect of melanocyte stimulating hormone on the reflectance of skin. The subject was seated beside a Cary model 14 reflectance spectrophotometer, and reflectance recordings were made of the extensor surface of the forearm and the mid-forehead, just above the glabella. The wave-length of incident light was varied from 700 mμ to 350 mμ. Duplicate tracings were made for each site

Subject J. R. Curve 1 was obtained before α-melanocyte stimulating hormone injections were given and curve 2 on the eleventh day of the experiment. The patient received on the first day, 3·1 mgm.; second day, 6 mgm.; third day, 9 mgm.; and up to the tenth day, 8 mgm. of α-melanocyte stimulating hormone a day. Note the decrease in reflectance throughout the spectrum

Subject E. C. received 8 mgm. of α-melanocyte stimulating hormone a day for ten days. Curve 1 was obtained on the first day and curve 2 on the thirteenth day. Note again the decrease in reflectance following administration of α-melanocyte stimulating hormone

Subject R. R. received 8 mgm. of α-melanocyte stimulating hormone a day for ten days. Curve 1 was obtained on the first day, curve 2 on the eleventh day. There was no change in reflectance during this period

Subject J. C. received 8 mgm. of β-melanocyte stimulating hormone a day for six days. Curves 1 and 2 were obtained on the first and seventh days. He then received 4 mgm. of α-melanocyte stimulating hormone for four days and 2 mgm. for one day. Curve 3 was obtained on the thirteenth day. There was definite darkening in this subject during administration of β-melanocyte stimulating hormone

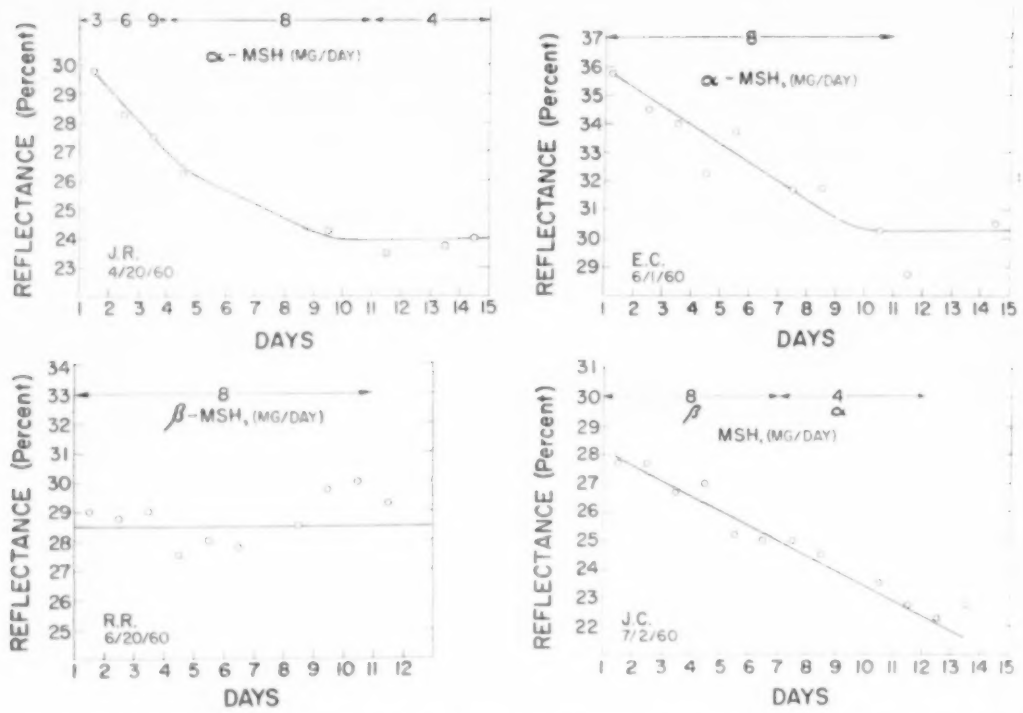


Fig. 3. Photovolt reflectance measurements during administration of melanocyte stimulating hormone. Reflectance of light from the skin was measured with a Photovolt model 610 photoelectric reflexion meter. The values used are arithmetic averages of separate readings made with red, blue, green and no filters. The forehead was measured in all patients except J. C., whose cheek was used. Here again it is seen that administration of α-melanocyte stimulating hormone to J. R. and E. C. resulted in a decrease in reflectance. Hog β-melanocyte stimulating hormone had no effect on R. R., but did cause a decrease in reflectance in subject J. C.

sodium, 141 m.equiv./l.; potassium, 4·7 m.equiv./l.; total protein, 8·5 gm. per cent; albumin, 3·2 gm. per cent; globulin, 5·3 gm. per cent; calcium, 12·1 mgm. per cent; phosphorus, 2·9 mgm. per cent; protein-bound iodine 7·8 μgm. per cent. On the fourteenth day these tests were repeated and found to be essentially unchanged: fasting blood sugar, 92 mgm. per cent; blood urea nitrogen, 12 mgm. per cent; carbon dioxide, 23·2 m.equiv./l.; chloride, 101 m.equiv./l.; sodium, 139 m.equiv./l.; potassium, 4·7 m.equiv./l.; total protein, 8 gm. per cent; albumin, 3·7 gm. per cent; globulin, 4·3 gm. per cent; calcium, 10·8 mgm. per cent; phosphorus, 3·4 mgm. per cent; protein-bound iodine, 7 μgm. per cent; erythrocyte sedimentation-rate, 7 mm./hr. The elevated globulin and calcium in the first group of studies suggested that the subject had sarcoidosis. However, X-ray examination of the chest was normal, and there were no symptoms or other signs of this disease. The activity of the synthetic α-melanocyte stimulating hormone was $3·3 \times 10^9$ units/gm. On the first day 0·1 mgm. of melanocyte stimulating hormone was given intravenously over a period of 5 hr. in a litre of 5 per cent glucose in water. There were no changes in blood pressure or pulse, and three additional injections of 1 mgm. each were given that day. Six injections of 1 mgm. each were given on the second day. On the third day the patient and his wife noticed darkening of his face which they described as grey. On this day he received a total of 9 mgm. in seven injections. On the fourth day there were four injections of 2 mgm. each. This dose of 8 mgm./day was continued through the tenth day with two injections daily. Then 4 mgm./day was given in two daily injections of 2 mgm. each for four days. No melanocyte stimulating hormone was given after the fourteenth day.

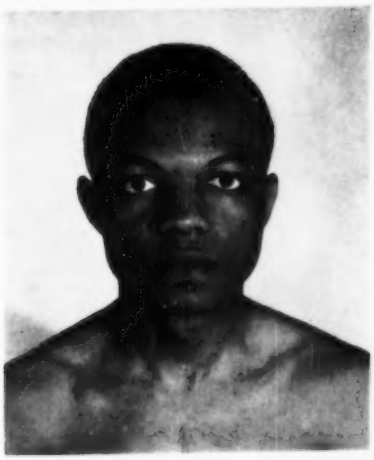
The first increase in pigmentation appeared bilaterally in roughly circular areas just above the zygoma. The pigmentation was not even initially; but after an additional four or five days blended into the surrounding skin colour. Six weeks after the termination of the injections the subject had returned to his original colour.

Subject 2. E. C., a 24-year-old hospital employee, was lighter than the first subject. His hyperpig-

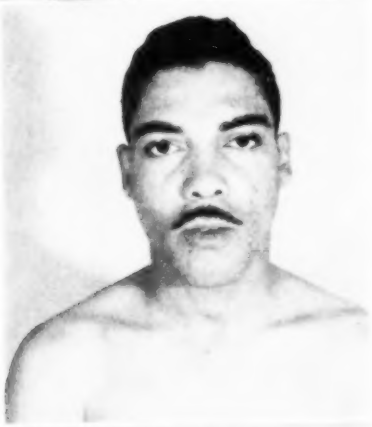
Plate (facing page). Appearance before and after administration of melanocyte stimulating hormone.
These photographs were made on Professional Ektachrome *E*-3, using an Eastman 81A colour correction filter. The lighting, shutter speed and diaphragm opening were not varied. The pictures of each subject were made on a separate roll of film. This helped eliminate variations due to developing. The photographs in all cases were made within 1 or 2 hr. of the Cary reflectance measurements in Fig. 2. The first picture was obtained just before treatment, the second picture just after treatment. The second picture of J. C. was made after β-melanocyte stimulating hormone and just before α-melanocyte stimulating hormone was given. There was darkening of both J. R. and E. C. following administration of synthetic α-melanocyte stimulating hormone. R. R. did not darken after he received hog β-melanocyte stimulating hormone, but J. C. did darken

J. R. 1

J. R. 2



E. C. 1



E. C. 2

R. R. 1

R. R. 2

J. C. 1

J. C. 2

J. C. 3

mentation following the administration of melanocyte stimulating hormone was not so pronounced to the eye. He received 8 mgm./day of synthetic α-melanocyte stimulating hormone for ten days in two daily injections of 1·0 ml. of gel. The activity of the melanocyte stimulating hormone was $3·3 \times 10^8$ units/gm. The melanocyte stimulating hormone used from the sixth to the tenth day had an activity of $2·0 \times 10^9$ units/gm.

Subject 3. R. R., age 25, received, in two daily injections, 8 mgm. per day of β-melanocyte stimulating hormone with an activity of $1·4 \times 10^9$ units/gm. for ten days. Routine analyses including blood count, urinalysis, blood urea nitrogen, fasting blood sugar, carbon dioxide, chloride, sodium, potassium, calcium, phosphorus and protein-bound iodine were normal on the first and last mornings of the test period. There was no observable or measurable darkening during the experiment.

Subject 4. J. C., age 23, received β-melanocyte stimulating hormone 8 mgm./day for six days in two divided doses daily. He darkened on this treatment. The β-melanocyte stimulating hormone had an activity of $1·3 \times 10^9$ units/gm. To test the effectiveness in this subject of α-melanocyte stimulating hormone ($2·0 \times 10^9$ units/gm.) which was more active than β-melanocyte stimulating hormone with regard to frog skin darkening, a smaller amount, 2 mgm./day of α-melanocyte stimulating hormone, was given for five days. There was some further darkening during this period.

It is interesting that the patients who darkened could detect the darkening at least as soon as we could measure it. This was attributed to the ability of the eye to integrate small changes in reflected light over a wide spectrum. The darkened skin had a decreased reflexion from 4000 to 7000 Å. Thus, melanin through its ability to absorb light of a large part of the spectrum is ideally suited for a light-protective role.

All subjects darkened more on the forehead than on the arm, and one (J. R.) showed quite striking darkening anterior to the ear above the zygoma. All hyperpigmentation had completely regressed within 6 weeks. The localization of the hyperpigmentation may result in part from the increased number of melanocytes present in the skin of the face[9].

From these experiments it is clear that systemically administered α-melanocyte stimulating hormone is an effective agent for darkening the skin of man. The relationship between melanin granule dispersion and new melanin formation in mammalian melanocytes is not known. However, since darkening begins almost within 24 hr., it is possible that dispersion of melanin granules occurs within the melanocyte similar to that seen in the pigment cells of frogs and fish following exposure to melanocyte stimulating hormone. Newly synthesized melanin, however, may account for the prolonged hyperpigmentation.

β-Melanocyte stimulating hormone from hogs was not effective in the first subject, but was effective in the second one. Each subject received β-melanocyte stimulating hormone that had been prepared in different laboratories. Both preparations of β-melanocyte stimulating hormone had almost the same activity on frog skin. It is not known whether the difference in darkening of human skin was due to some unknown variation in the two β-melanocyte stimulating hormones or to a difference in response of the two subjects. Human β-melanocyte stimulating hormone was not available for testing. Neither α- nor β-melanocyte stimulating hormones had any effect on numerous metabolic tests carried out.

There is still doubt whether adrenocorticotrophic hormone can darken human skin. When this hormone was first introduced to clinical medicine approximately ten years ago, it was not uncommon to see patients develop pronounced hyperpigmentation following its use. These older preparations of adrenocorticotrophic hormone contained large amounts of melanocyte stimulating hormone[1]. More recently, commercial adrenocorticotrophic hormone has had much less melanocyte stimulating hormone, and the hyperpigmentation that occurs is less frequent and less pronounced. It would be possible to give 100–200 units of adrenocorticotrophic hormone free of melanocyte stimulating hormone to an experimental subject in order to test the effect of homogeneous adrenocorticotrophic hormone on skin darkening. With regard to darkening frog skin, this amount of adrenocorticotrophic hormone would be very small compared with the melanocyte stimulating hormone given the four subjects described in this report. On frog skin adrenocorticotrophic hormone has only one-thirtieth the activity of α-melanocyte stimulating hormone. Thus the amount of melanocyte stimulating hormone used daily in the present studies would equal more than 25,000 units of adrenocorticotrophic hormone in frog skin darkening activity. Perhaps some day it will be possible to give α-melanocyte stimulating hormone from which the N-terminal acetyl group is removed. The darkening action of this peptide might be like that of adrenocorticotrophic hormone which also has a free N-terminal serine.

One can ask whether the 4–8 mgm. of α-melanocyte stimulating hormone which was injected daily is a physiological amount of this hormone. Without knowing the amount of the injected material that is destroyed or sequestered by muscle and the amount normally produced by the human pituitary, this question cannot be resolved. All work carried out thus far has given results consistent with the view that the hyperpigmentation seen in patients with adrenocortical insufficiency and in some patients with pituitary tumours could be due to an increased release of α- or β-melanocyte stimulating hormone or both from the pituitary gland into the general circulation.

This work was supported by a grant from the U.S. Public Health Service, and during the tenure of a special fellowship from the National Institute of Arthritis and Metabolic Diseases, U.S. Public Health Service held by one of us (J. S. McG.).

We wish to thank Dr. M. Ruth Wright, who carried out the bioassay for α- and β-melanocyte stimulating hormones.

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POSSIBLE BIOLOGICAL EFFECTS OF ELECTRICALLY CHARGED PARTICLES IN TOBACCO SMOKE

By Dr. K. H. KINGDON

General Electric Research Laboratory, Schenectady, New York

THE idea that inhaled atmospheric ionization may have some effect on humans has been current for about thirty years. Recent experiments by Krueger and Smith[1] have demonstrated that air ions incident on the mammalian trachea will increase or decrease the vibration frequency of the cilia according as the ions are negative or positive. I have pointed out[2] that 'glow discharge electrolysis' experiments[3,4] indicate that the ordinary 'small ions' of atmospheric electricity carry appreciable quantities of chemical and electrostatic energy (about 6 eV./ion), and I have found that 5×10^{-4} coulomb/sq. cm. of such ions incident on *Escherichia coli* will kill them to 1/*e*. This amounts to 3×10^{5} ergs/gm. and is about eight times the amount of ultra-violet energy or 700 times the amount of X-ray energy required to kill *E. coli*.

With the establishment of definite biological effects of atmospheric small ions such as those referred to above, it becomes of interest to inquire whether the ions which are well known to be present in tobacco smoke are of such a kind, or are present in sufficient numbers, as to produce significant biological effects when inhaled.

Ions in Smoke from Tip of Cigarette

Ions from the cigarette were analysed by drawing them in a current of air through the standard mobility equipment of atmospheric electricity, the particular apparatus being operated so as to collect small ions of mobility greater than 0·4 cm.^{2}/sec. volt and to reject slower ions. The sum of large and small ions was measured, without analysis, by other equipment. Air was drawn through the cigarette as needed with equipment giving a 'standard draught' of 35 c.c. in 2 sec. The ambient air currents at the cigarette tip were gentle enough so that after initial ignition a 'king-size' cigarette required 14 min. to burn up, without further 'standard draughts'. The ions are presumably generated by thermal ionization of potassium, which is always present in substantial amounts.

The first attempts to observe small-ion currents from a burning cigarette showed that small ions were indeed generated, but in numbers which increased greatly with application of a few hundred volts, or more, to the mouth end of the cigarette. The applied voltage creates a field at the burning tip which separates the positive and negative ions generated there and prevents their rapid recombination. Simple measurements show that a smoker's ordinary movements will raise his body to potentials of hundreds of volts, so that an adequate voltage is often applied automatically to the cigarette.

Fig. 1 shows the small-ion current as a function of voltage applied to the mouth end of a burning cigarette. At a few hundred volts the current is of the order of 10^{-10} to 10^{-9} amp. The current increases systematically with voltage, but shows a marked saturation trend above 1,000 V.

In addition to the emission of small ions, there is an emission of large ions which is about an order of magnitude greater than the small-ion current. The currents of both large ions and small ions increase sharply when the temperature of the cigarette is raised by giving it a standard draught. Both currents also increase sharply when ash is removed so as to expose the burning area.

The saturation behaviour of the small-ion current is due to the high electrical resistance of the cigarette. It was found that the resistances of a number of unlighted cigarettes were of the order 10^{10}–10^{11} ohms, and that although the resistance of the cigarette was lowered temporarily by taking a standard draught, the resistance returned to a high value between draughts.

Fig. 2 shows the variation with time of the emission of small ions from a cigarette charged to 1,000 V. after one standard draught only. The emission fluctuates down and up as ash accumulates or is removed by natural fall and by tapping. It is clear that the cigarette is a continuous source of small ions of the order 3×10^{-10} amp.

Ions are present in the smoke drawn through the cigarette and increase in number as the electric field

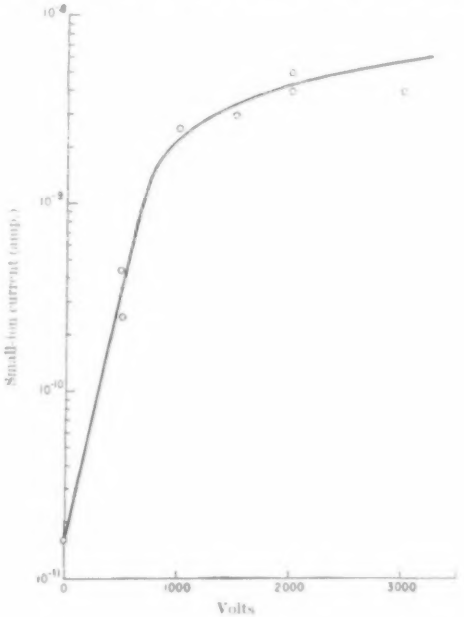

Fig. 1

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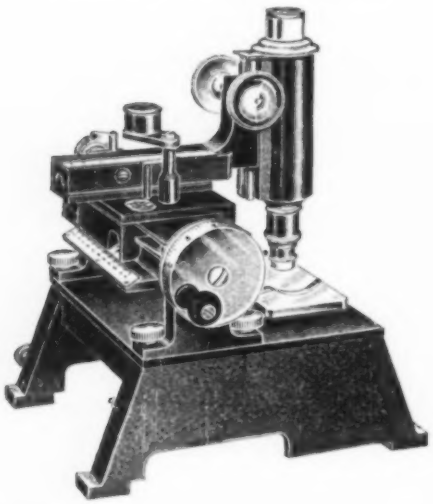

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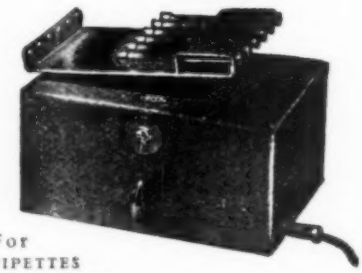

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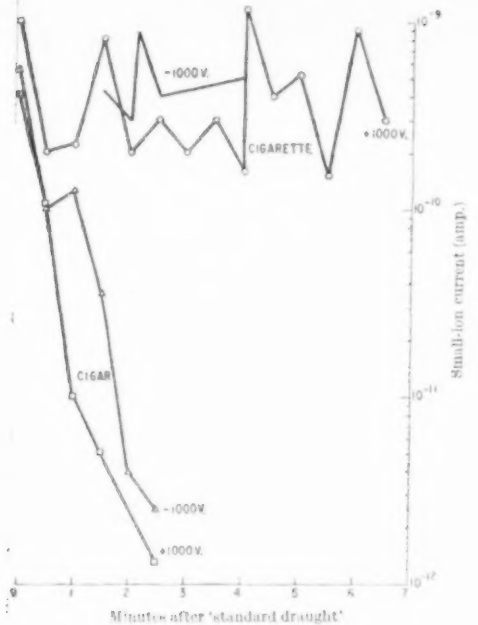

Fig. 2

at the burning tip is increased. No small ions could be detected in this smoke stream. In a more rigorous test of this sort, small ions generated by electrical corona were used. It was found that passing this ion stream through a 1-cm. length of cigarette reduced the small-ion content to 1/3,400, and passing it through 0·7 cm. of filter tip reduced the small-ion content to 1/8,500. The conclusion from these tests is that any small ions generated at the burning tip are removed (to about 1/10,000) by Brownian movement and electrical forces on their way through the cigarette and do not enter the mouth. The large ions, formed by coalescence of small ions with smoke particles, are thought not to have any specialized biological effect ascribable to their charge[2].

Unipolar small ions leaving the tip of a charged cigarette are spread throughout a substantial volume by thermal or air current convection, by motion of the cigarette, and by their mutual repulsion. The repulsion limits the concentration of unipolar ions which can be built up in the vicinity of the cigarette. Thus if N positive ions of charge e are within a sphere of radius 25 cm., the electric field Ne/r^2 at the surface of the sphere for $N = 1{\cdot}8 \times 10^{10}$ will be 4 V./cm. The ions at the surface of the sphere will move outwards with a velocity of 4 cm./sec., about twice that given to them by the ordinary atmospheric electric field. The average concentration in the sphere of radius 25 cm. is $2{\cdot}8 \times 10^5$ ions/c.c. It appears that the generation of small ions by the cigarette can maintain a concentration of this order, but it also appears that repulsive forces will prevent the concentration from being much higher.

It seems likely, therefore, that a smoker inhales small ions at a concentration of approximately 2×10^5 ions/c.c. all the time that he is smoking a cigarette. This concentration is about one thousand times that found in an ordinary city bedroom with no smoking going on.

Similarities between Experimental Small-ion Effects and Alleged Correlations of Smoking with Lung Cancer

The discussion so far has dealt with the physical characteristics of the emission of small ions from a burning cigarette. The remainder of this article will be devoted to an exploration of the possible relation between continued inhalation of super-normal quantities of small ions and the development of lung cancer. This hypothesis is envisaged as an alternative to the concept that lung cancer may be caused by carcinogenic chemicals in tobacco smoke. The carcinogenic chemical concept is not universally accepted[5,6] as a major cause of lung cancer, so it seems worth while to explore an alternative. Explanations offered by this alternative hypothesis for three areas of observation in smoking and lung cancer will be compared first.

Comparison of cigarette, cigar and pipe smoking. Evidence has been presented in the literature which is alleged to show that lung cancer is much less frequent among cigar and pipe smokers than it is among cigarette smokers. Data have been presented in the present article to show that a charged, burning cigarette is a relatively strong and continuous source of small ions. Similar tests with a cigar showed that although a vigorously smoked, charged cigar (two successive standard draughts) gave transient small-ion currents comparable with those from a cigarette (see Fig. 2), the current decreased rapidly with time, so that a cigar is a much weaker continuous source of small ions than a cigarette. Similar tests with a charged pipe showed it to be an even weaker source.

Alleged differences between the behaviour of cigarettes, cigars and pipes in producing lung cancer may thus be correlated very simply with observed differences in the numbers of small ions produced.

Site of lung cancer as observed in diagnosis. The type of lung cancer which is alleged to be connected with smoking is observed first in the lower parts of the bronchi. Particles capable of rapid diffusion, such as the small ions, are much more likely to be deposited in the bronchi than are the slow, 0·5 micron droplets, carrying the alleged carcinogenic chemicals.

Failure to give mice lung cancer by inhalation of smoke from a smoking machine. Several attempts have been made to develop lung cancer in mice by exposure to smoke from a smoking machine[7], but in such experiments the development of cancer has not exceeded the normal expectancy. It has been pointed out above that by passage through the cigarette small ions are completely removed from the smoke of even a strongly electrically charged cigarette, so that the mice, although possibly exposed to inhalation of carcinogenic chemicals in the smoke, were not exposed to the effects of any small ions which may have been created initially in the smoke.

Possibility of Biological Damage from Inhalation of Small Ions

Data are not available to permit a convincing calculation of the possibility of lung damage resulting from inhalation of small ions in cigarette smoke. However, it is worth noting that the biological effect of small ions is closely similar[2] in most details to the familiar indirect X-ray process of radiation biology. Both processes involve the initial formation of a positive ion and a free electron, which afterwards give rise to active chemical species. The chemical energy

of these secondary products causes the final biological effect. In view of the major similarity between the two processes, it seems reasonable to put forward as a hypothesis that if prolonged exposure to a low intensity of X-rays or other ionizing radiation can cause lung cancer, prolonged exposure to small ions at an intensity about one hundred times normal may also cause lung cancer.

It should be emphasized, however, that as yet there is no experimental demonstration of this, and the small-ion hypothesis is simply advanced as an alternative approach which appears to merit further exploration.

The emission of small ions from a charged, burning cigarette can be completely suppressed by smoking the cigarette within a screen which always encloses the burning tip and maintains zero field there. Suppression of emission of small ions is complete even when cigarette and shield are charged to 3,000 V. If further experimentation confirms the hypothesis of the production of lung cancer by small ions, it would be very satisfactory to have available such a simple and effective means of suppressing the effect.

Since potassium, or some other element of low ionization potential, is probably intimately connected with the formation of the small ions by thermal ionization, elimination of this element from tobacco presumably would reduce greatly the generation of small ions from an unshielded cigarette.

I am indebted to the General Electric Research Laboratory for making laboratory facilities and equipment available for carrying out the work just after my retirement. I wish also to express my appreciation to C. M. Bishop for continued help with the experiments, and to H. Hurwitz, jun., J. L. Lawson and J. K. Bragg for constructive criticism.

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CENTENARIES

By JOAN M. EYLES

Samuel Clegg, 1781–1861

SAMUEL CLEGG the elder, a pioneer gas engineer, died at Haverstock Hill, Middlesex, on January 8, 1861, within two months of his eightieth birthday. Clegg was born in Manchester and received some of his education from John Dalton, who was teaching in Manchester from 1793 onwards. About this time William Murdock was carrying out his first experiments in gas-lighting while he was employed by the Birmingham firm of Boulton, Watt and Co. When young Clegg later became apprenticed to this firm, they were developing their first gas-making plants. It is not surprising, therefore, that his interests turned in that direction.

He left the firm in 1805 to set up in business himself, and soon after installed gas-lighting in the cotton mill of Henry Lodge at Sowerby Bridge, near Halifax. In 1808 he was awarded a silver medal by the Society for the Encouragement of the Arts for his apparatus for making gas from pit coal and lighting factories therewith. Later on he moved to London, and in 1812 installed gas-lighting in both the dwelling-house and business establishment of Rudolph Ackermann, the well-known art publisher, at 101 Strand.

In 1812 the Gas, Light and Coke Company obtained a charter to operate in the metropolis, and a few months later Clegg became its chief engineer. He was with the Company for nearly five years, and undoubtedly its success owed much to his ability. Clegg was responsible for the lighting of Westminster Bridge in 1813 (even lighting the lamps himself when the lamplighters refused to risk it) and also for the installation of gas mains along many of the streets of Westminster and the City. A notable achievement was the lighting of Guildhall in the City, inaugurated on November 9, 1815. During this period he introduced many improvements, including the first gas-meter and a gas governor; he also designed a horizontal rotary retort, which was incorporated in the plant installed at the Royal Mint by F. Accum, in 1817, the year in which Clegg left the Gas, Light and Coke Company.

Clegg afterwards suffered financial reverses. He worked for a time as engineer to the Portuguese Government, and also became involved with a project for a so-called atmospheric railway, in which a vehicle attached to a piston in a continuous pipe is made to move by maintaining a low pressure on one side of the piston. Later, however, he received a Government appointment as a gas surveyor, and also assisted his son, Samuel Clegg the younger, with the preparation of a treatise on the manufacture of coal gas.

Sir James Hall (1761–1832)

SIR JAMES HALL of Dunglass, fourth baronet, was born on January 17, 1761. He succeeded to the title when only fifteen, on the death of his father, Sir John Hall. In 1784 he was elected a member of the recently founded Royal Society of Edinburgh, a society with which he was closely connected for the rest of his life, publishing his scientific and literary papers in its *Transactions*, and holding office as president during 1812–20.

When Hutton's famous paper on a "Theory of the Earth" was read to the Society in 1785, Hall was abroad, studying among other matters the lavas of Vesuvius. At that time he was not attached to any system of geology, but later was won over to the Huttonian system and then became one of its most ardent supporters. He saw the possibility of testing the validity of some of Hutton's ideas by laboratory experiment, but this suggestion was not welcomed by Hutton himself; and it was only after the latter's death in 1797 that Hall began to carry out experiments seriously and systematically.

In 1798 he showed that glassy material obtained by heating strongly different lavas and whinstones would revert to a crystalline material if cooling was

sufficiently slow. He followed these experiments with others designed to show the "Effects of Compression in modifying the Action of Heat", in which his aim was to demonstrate that when powdered limestone was strongly heated it would, if heated in a confined space, fuse and re-crystallize instead of decomposing. Using gun-barrels and other apparatus of his own design, he succeeded in his objective, obtaining results on which subsequent experimenters were unable to improve substantially for nearly a century, and which clearly show his skill and perseverance at a time when pyrometry and furnace control were in their infancy. Indeed, he opened up an entirely new field of research in chemistry and geology.

Hall's interest in experimental geology continued through his lifetime, and he investigated the effect of lateral compression on bedded strata, and the causes of consolidation of strata. After his death in 1832 some of his apparatus and a number of specimens were presented to the Geological Society of London by his son, Captain Basil Hall, and they are now in the collections of the Geological Museum.

OBITUARIES

Prof. G. W. O. Howe

THE initials G.W.O.H., familiar to radio engineers throughout the world, passed from currency on November 7 with the death of Prof. George Walter Osborne Howe.

Howe, who was born on December 4, 1875, at Charlton, Kent, and educated at the Roan School, Greenwich, took pride in the long association of his family with riverside London. His forebears were, he used to say, Thames watermen.

After an engineering apprenticeship with Siemens Brothers in Woolwich, Howe became an undergraduate at Armstrong College, Newcastle on Tyne. He graduated with honours from the University of Durham in 1900 and he had the distinction of being the senior Whitworth Scholar in that year.

During 1900–02 he obtained experience in the design of electrical machines at the Siemens-Schuckert works in Berlin, this incidentally being a period in which the German designers of electrical machines were pre-eminent in Europe.

On his return to England, he took up his first teaching appointment in the Hull Technical College, and apart from a brief interlude in 1920–21 at the National Physical Laboratory, where he was head of the Department of Electrical Standards and Measurements, the whole of his long career was devoted to academic work.

It was in 1905 that he was appointed to a lectureship in the City and Guilds College, and there he began to make his major contributions to electrical science. His most notable original work was on radio propagation, the behaviour of radio aerials and on the penetration of high-frequency currents into conductors. His earliest papers show that distinctive quality of mind which was to characterize all his publications and to bring to him in later years a reputation which was truly world wide. His intellectual armoury comprised a superb knowledge of classical electromagnetism, exceptional powers of physical visualization, and the capacity to devise new methods of approach to complex phenomena whereby familiar concepts and relatively simple mathematical methods could be applied.

During 1910–20 he contributed to *The Electrician* a series of papers dealing in the main with high-frequency phenomena, and he made communications on the same subject to the *Proceedings of the Royal Society* and to the *Journal of the Institution of Electrical Engineers*.

In 1921 he was appointed to the newly created James Watt chair of electrical engineering in the University of Glasgow. At about the same time the monthly journal *Experimental Wireless*, now *Electronic Technology*, invited Prof. Howe to become its technical editor. This editorship, which lasted for more than twenty-five years, must be one of the most remarkable in the history of scientific publishing. Every month an editorial appeared over the initials G. W. O. H. Just occasionally the editorial would be of conventional form, commenting in a general way on some development or perhaps on an international conference. The regular pattern was, however, a closely reasoned exposition of some piece of electrical theory relating to a topic of current interest. The article might expose a fallacy, might derive by a brilliant simplification a result obtained in some recently published paper by a recondite method, or might treat a difficulty which had arisen in the course of discussion with his colleagues. Many of the problems which he tackled involved conceptual difficulties of a high order and he would admit to many hours of anxious thought over some of them and, on one or two occasions, to momentary misgivings after he had gone to press. In these editorials, not only was his capacity for clarity of exposition displayed at its best, but also his genius for the apt simile and for witty and sometimes caustic comment had free play. Muddled thinking or obfuscation would sometimes provoke him to a sharpness of witty sarcasm which could give a false impression of him.

Quite early in his career he began attending meetings of the British Association. He became, in due course, secretary and afterwards recorder of Section G (Engineering), and in 1924 president of that Section. He attended three of the meetings which the British Association held overseas—Adelaide in 1914, Toronto in 1924 and Johannesburg in 1929. In January 1938 he went as a member of the official delegation of the British Association to the jubilee meeting of the Indian Science Congress which was held in Calcutta.

During the later part of his life he maintained a direct association with the radio-manufacturing industry as a director of the Mullard Radio Valve Company.

Prof. Howe was elected to associate membership of the Institution of Electrical Engineers in 1905. He took a prominent part in the formation of the Wireless Section of the Institution in 1919 and he was elected chairman of the Section in 1921. In 1956 the Institution awarded to Prof. Howe the Faraday Medal in recognition of his pioneering work in the study and analysis of high-frequency oscillations and

of the theory of radio propagation and for his outstanding contributions to engineering education. The Institute of Radio Engineers of New York in 1955 also conferred on him the high honour of election to fellowship of the Institute.

His scientific work apart, Howe experienced his greatest enjoyment in his music. He was an accomplished violinist. He had been taught, he said, when very young on a miniature violin specially made for him, and he could not remember a time when he did not play the instrument. Until a year or two before his death he was an active member of the Glasgow University Orchestral Society.

Only those who had the good fortune to study under him knew the quality of his teaching. He was one of the greatest teachers of his generation. It is hard to escape the conclusion that the main driving force in his scientific work was the urge first to understand, in Clerk Maxwell's boyish phrase, "the go of the thing" and then to expound it. His mind was essentially scholarly, and yet one got the impression that he was intrigued by the unexpected practical implication, the apparent anomaly or the amusingly odd concept rather than by the deeper philosophical implications.

A lively and entertaining companion, a delightful host and an equally delightful guest, Prof. Howe had a wide circle of friends. It was only rarely that the brilliant mind, which in its day-to-day contacts with the world gave the impression of being quietly but confidently self-contained, revealed for a moment that depth of human feeling of which it was capable.

Prof. Howe married in 1901 Sarah Alice Maunder. Mrs. Howe died in 1930. J. Greig

Dr. Norman Bauer

Not often is exceptional scientific ability and a deep concern for the welfare of his fellow man combined in one individual. Such an individual was Dr. Norman Bauer.

Dr. Bauer began his studies at the University of California at Berkeley, graduating with a B.S. in chemistry in 1937. He then entered the University of Michigan, receiving his M.S. in 1939 and his Ph.D. in 1941, under the direction of Prof. K. Fajans. He held a scholarship during 1936–37 at the University of California and was Eastman Kodak Fellow at the University of Michigan during 1940–41, and a Post-doctoral Fellow at that institution during 1941–42.

Desiring to teach, he joined the faculty of the University of New Hampshire in 1942 and remained there until 1945. During this period he was co-author with Prof. Fajans of the sections on the determination of density and refractometry in Weissberger's *Technique of Organic Chemistry*, having done much important research in these fields. Due to personal obligations, he returned to California in 1945, where he was employed by the California Research Corporation. Here he became interested in mass spectrometry, publishing articles in this field. In 1949 he founded an independent research laboratory under the name Physical Science Associates at Berkeley. Later, with his personal obligations changed, he returned to academic life, accepting a position at Utah State University in 1953, where he was most recently professor of chemistry.

Here he carried on an excellent programme of teaching and basic research in physical chemistry. His knowledge and enthusiasm encouraged research in several fields, and many new methods of approaching problems in soil and plant nutrition and in the thermodynamics of the water relations of soils and plants were developed by him. He became interested in the problem of biological nitrogen fixation and made substantial progress in this difficult field, studying the physical chemistry of legoglobins (the proteins involved in nitrogen fixation), establishing a reputation for his laboratory in this topic. Recently, he made significant discoveries that may lead to a major advance in the solution of this problem. Working with electron spin resonance equipment at Varian Laboratories during the summer of 1960, he detected the presence of free radicals that could be key intermediates in nitrogen fixation. This was especially gratifying to him, since he had predicted theoretically the existence of such radicals in a study of possible pathways for the process. His death on September 9 prevented him from following up this important possibility.

Dr. Bauer was concerned about many problems involving man's welfare. He was opposed to further testing of atomic bombs and personally paid for advertising space to register his protest. He published articles questioning the reasoning of the U.S. Atomic Energy Commission on the hazards of radioactive fall-out. He was particularly concerned with the dangers of nuclear war and spoke out strongly for the cause of peace. He was a champion of the cause of academic freedom, taking an active part in upholding the right of free inquiry. A dedicated scientist, a gifted teacher, he was, in every sense, a man of unquestioned integrity and morals who brought honour to his profession, and a man of good will. Jack T. Spence

Mr. Jaques Cattell

Jaques Cattell, editor of *American Men of Science*, publisher of the *American Naturalist*, and president of the Jaques Cattell Press, Inc., died after a long illness at New York Hospital on December 18; he was fifty-six years old.

In 1923 Mr. Jaques Cattell became associate editor of *American Men of Science* with his father, the late Dr. James McKeen Cattell, and editor following the death of his father. He was also editor of *Leaders in Education*, founded by his father. The *Directory of American Scholars* was established by him in 1942, under the sponsorship of the American Council of Learned Societies.

Mr. Jaques Cattell was interested in scientific publishing and the graphic arts. He was president of Science Press Printing Company, and later was a pioneer in the use of cold type composition in scientific publishing. In 1959 he moved to Arizona, and, at the invitation of the President of Arizona State University, continued the publication of his biographical directories from the University campus in Tempe.

He is survived by his widow, the former Elizabeth Walsh, and his son, James Cattell.

The Jaques Cattell Press, Inc., has announced the appointment of Garrison Cattell and Dorothy Hancock as acting editors of *American Men of Science*. Mr. Cattell and Mrs. Hancock have worked closely with Mr. Jaques Cattell in editing and publishing this directory.

NEWS and VIEWS

Mathematics at Canberra : Dr. B. H. Neumann, F.R.S.

Dr. B. H. Neumann has been appointed to the newly established chair of mathematics at the National University of Australia, Canberra. Bernhard H. Neumann was born in Berlin in 1909. He received his early academic training at the Universities of Freiburg and Berlin, where he obtained the degree of Dr. phil. in 1932. Soon afterwards he left Hitler's Germany and continued his research work at Cambridge, where he graduated Ph.D. in 1935. His first teaching appointment was at University College, Cardiff (1937–40). This was followed by war service from 1940 until 1945. After the War he joined the staff at University College, Hull (1946–48). Since 1948, Dr. Neumann has been a member of the Mathematics Department at Manchester, first as a senior lecturer and later as a reader. Neumann's published work is almost exclusively devoted to the theory of groups. He has enriched this important branch of modern algebra by outstanding contributions published in numerous articles, in which he lucidly expounds his results, solves old problems and poses new ones. His achievements have been recognized by academic distinctions which include the Adams Prize (1951–52), the D.Sc. degree at the University of Manchester (1954) and the election to the Royal Society (1959). Besides his creative powers, Dr. Neumann possesses a remarkable talent to inspire young mathematicians and to guide them through all the stages of their career as research workers. He will no doubt attract to Canberra a team of enthusiastic collaborators. Chief among these will be his wife, Dr. Hanna Neumann, who is well known for her own work on group theory.

Engineering Science at Oxford : Prof. A. Thom

Prof. A. Thom is to retire from the chair of engineering science at the University of Oxford, which he has held since 1945. Prof. Thom is an engineer with an aeronautical bias, who worked in the Royal Aircraft Establishment, Farnborough, during the whole of the Second World War, after a long period as a lecturer at the University of Glasgow. He is best known for his skill and inventiveness in the field of numerical analysis by desk computers. In particular, he has obtained a large number of useful results in theoretical fluid dynamics and other subjects by his 'squares' method, an alternative to Southwell's 'relaxation' approach. He is also well known for a number of important wind-tunnel investigations.

Prof. D. W. Holder

Dr. D. W. Holder, who is to succeed Prof. Thom in the chair of engineering science at the University of Oxford, is like him in that he is an aeronautical engineer, who has built up since the War a remarkable research team in high-speed aerodynamics at the National Physical Laboratory. This team has been responsible for a large proportion of the fundamental advances in transonic, supersonic and hypersonic gas dynamics in Britain since 1945. The research facilities which he has built up have been truly impressive, but his contributions towards interpretation of the results have been equally important, notably in the field of shock-wave boundary-layer interaction.

Current Research and Development in Scientific Documentation

A recent issue of *Current Research and Development in Scientific Documentation*, issued by the National Science Foundation, lists 159 research projects in 99 organizations, compared with 61 in 39 organizations a year ago (No. 7. Pp. viii+153. Washington, D.C.: Government Printing Office, 1960. 65 cents). Of these 17 are listed under information requirements and uses; 45 under information storage and retrieval; 26 under mechanical translation; 17 under equipment; and 54 under potentially related research which is not directly connected with scientific documentation, but which may influence such work in the future. The present issue is provided with a detailed subject index and an introductory statement to each section directing attention to new work and to closely related projects reported in other sections. In the first section may be noted the study by the International Federation of Documentation of the availability and value of scientific conference papers and proceedings; a study of the availability and publication of scientific information contained in unclassified Government research reports; studies of the use of photocomposition and of microform publication, of the information needs of scientists in the field of psychopharmacology and of the need for an abstracting service in soil and water technology. In information storage and retrieval most of the effort is concentrated on systems design, but there is growing interest in evaluation and comparison of the newer systems, in more theoretical work on systems design and in mechanized processing of complete texts. Mechanical translation research up to the present has been mainly concentrated on the problems of lexicon and the passing of the source languages, principally Russian and English, with relatively little attention to the synthesis of the output language. The most noticeable trends are the increasing number of languages under study and the increasing breadth and generality of the theoretical work. Under equipment, particular emphasis is being placed on the development of storage devices and of output components.

Education and Industry

In an article that appeared in a recent issue of *ESSO Magazine* (9, No. 4, Autumn, 1960), Sir Hugh Beaver suggests that people in Great Britain can no longer afford to argue about education for management, and that it is no longer realistic to call on "industry to exercise the greatest care in recruiting graduates", in order to allow the schools to have a proportion of the 'good people' for advanced studies. He argues that to many, what matters are the financial attractions, and says that no one should question or deplore such an attitude in any individual, now that it has been shown that industry offers as

great an opportunity of real service to the community and to the country as any of the professions. There are many thousands of companies in industry and commerce who want an educated intake but who are harassed by the deficit due to a shortage of teachers. Such difficulties could be solved, he suggests, by a system of senior part-time appointments or temporary secondments, or by alleviating the problem of the shortage of teachers itself. However, he directs attention to the fact that it cannot be claimed that we are deploying Britain's full resources so long as women play such a small part in our industrial, scientific, technological and high-management activities. Sir Hugh also touches on the increasing specialization which now occurs right through industry. These specializations are now acceptable, and the formal ladder of promotion and success must be by one or other specialization. The great task that confronts all who are training managers is to produce people who, while initially master of one or other specialization, can at the same time understand how the other parallel and complementary specializations all build the one body, whether it is their own company or the industry of which their company is a unit. Only by such means will they be capable of becoming managers with wide responsibilities.

Mental Health

During 1959–60 the major concern of the National Association for Mental Health has been with the promotion of World Mental Health Year in the United Kingdom and with preparations for the coming of the Mental Health Act. These are described in the fourteenth annual report (Pp. 55. London: National Association for Mental Health, 1960). Before the Mental Health Act received the Royal Assent on July 29, 1959, the Ministry of Health had issued circulars in anticipation of its coming. The most noticeable was that issued during January 1958, authorizing the informal admission of patients to mental deficiency hospitals. Following the passing of the Mental Health Act, the Minister of Health issued a direction to local authorities asking them to submit details of their proposals for community care. These are now being studied at the Ministry. Another development of considerable importance to the Association is the initiative of the Royal College of Nursing in petitioning the Privy Council for an alteration in its Charter to enable all registered nurses to become members of the College. If the petition is granted, mental nurses, male and female, may, for the first time, become members of the Royal College of Nursing. Information about the work of the Association can be obtained from Maurice Craig House, 39 Queen Anne Street, London, W.1.

Polish Scientfic Publications

The *Quarterly Review of Publications*, published since 1955, describes publications of the Polish Academy of Sciences and of such scientific societies as are supported by the Academy. For the convenience of readers interested in particular disciplines, the *Review* has appeared since 1958 in three series: Series *A*, Social Sciences; Series *B*, Biological Sciences; and Series *C*, Pure and Technical Sciences. To give the reader a more complete picture of current Polish scientific literature, the editors have decided to include in the *Review* the more important scientific publications of institutions other than the Polish Academy of Sciences and the affiliated societies. Each entry published in the *Review* is supplemented by a brief summary. Titles are quoted in the language used by the author and, except in the case of Latin and Greek titles, an English translation is given. Copies of the *Review* can be obtained from the Distribution Centre, Warszawa, Palac Kultury, I, Nauki.

Peabody Museum of Yale University

The annual report of the Peabody Museum of Yale University for 1960 is unusual in that it is the first to be issued by the Museum and is also the first by the present director, Mr. S. Dillon Ripley (Pp. 31. New Haven, Conn.: Peabody Museum of Natural History, Yale University, 1960). It also coincides with the re-activation of the Museum Trustees and the Advisory Committee. The report records the opening of the new wing on October 30, 1959, which event marked the culmination of nearly 15 years planning. The director rightly states that the health of a museum depends not only on the development of exhibits, or the active progress of school services, but also on the calibre of the research by the staff and those associated with it. An impressive list of publications is a measure of the research carried out by this Museum. It is intended that reports should include semi-popular articles on natural history subjects—the first one being on the wren.

The Australian Museum

The first part (two stories) of the new six-storey wing of the Australian Museum was officially opened by the Premier of New South Wales, Mr. R. J. Heffron, on August 11. The completion of this first part is one of the outstanding events in the history of the Museum, for it is the first major building addition for half a century. The new work is faced with handsome sandstone and contains curatorial offices, laboratories and space for reserve collections. The contract for the erection of the other four floors has already been signed and these will enable further collections to be displayed and also provide for a public cafeteria on the roof.

Impact of *Lunik* 2 on the Moon

At about the time when *Lunik* 2 struck the Moon, 21h. 02m. 24s. U.T. on September 13, 1959, optical observers in several parts of Europe noted small disturbances on the Moon's surface. Their observations, none of which could be certainly linked with *Lunik* 2, were reviewed by G. Fielder (see *Nature*, 185, 11; 1960). One group of observations, from Hungary, has now been described in more detail by L. Detre, in a publication entitled "Bericht über Optische Beobachtungen Anlässlich der Landung der Sowjetischen Mondrakete Lunik II" (Mitteilungen der Sternwarte der Ungarischen Akademie der Wissenschaften. Nr. 45: Pp. 10. Budapest: Sternwarte der Ungarischen Akademie der Wissenschaften, 1960). On the night of September 13, which was exceptionally clear in Hungary, an expanding dark spot was observed on the moon, near the crater Autolycus, by several astronomers at two independent observatories, Szabadsághegy and Baja, between the times 21h. 02m. 30s. U.T. and 21h. 07m., when it became too diffuse to observe. Traces of a similar phenomenon were found on photographs taken at the same time at Uppsala, Sweden. The co-ordinates of the dark spot ($+0{\cdot}03$, $+0{\cdot}45$) agree well with those given for the impact point of *Lunik* 2.

Seventeenth-Century Bronze Finds in Eastern Nigeria

An interim report of excavations undertaken at Igbo-Ukwu, Eastern Nigeria, by Thurstan Shaw, appears in the November issue of *Man*. About twenty years ago some interesting finds, including bronze vessels, were unearthed by an African called Isaiah Anozie when digging out an underground cistern. Some of these objects are now in the museums at Jos and Lagos, and the facts of the find were duly reported in *Man*. Thurstan Shaw has now undertaken systematic investigations at the site and many more objects have been recovered from this and another nearby compound. They include pots, bowls, a swordhilt and scabbard, ornaments, rings, and a coiled snake on a spike, all in bronze. Of the two sites the first seems to have been a vessel or regalia store-place, and the second a burial. It is suggested that they were both connected with the former *Eze Nri*—the priest King of Umueri, who brought from the region of Idah an intrusive culture into Iboland. A seventeenth-century date and African workmanship are here tentatively postulated.

Indians of the Western Prairies

The Department of Northern Affairs and National Resources, Canada, has recently issued a bulletin in its Anthropological Series entitled *Indian Days on the Western Prairies*, which has been prepared by Marius Barbeau (Bulletin No. 163. Anthropological Series, No. 46. Pp. vi + 234 and 165 plates. Ottawa: Queen's Printer, 1960. 4 dollars). The Bulletin is full of Indian tales and is well illustrated, sometimes in colour. But the work, of course, is a serious contribution to the study of the old inhabitants of the western prairies. There is a long introduction, where a general account of the tribes and their problems is given and the difficulties facing them are discussed. Most of the volume, however, is devoted to stories told by the Indians themselves, which give a vivid idea of the outlook on life of these people at the time of the coming of the white man, and of how they reacted to his arrival. There are a great number of illustrations of scenes and designs, mostly taken from paintings on skins. There are also portraits drawn in characteristic style by Langdon Kihn. The volume is of great value to anyone wishing to learn something of the civilization of these interesting peoples.

Diagnosis of Yaws

As increasing progress is made in the eradication of yaws in many countries, it becomes increasingly important to differentiate as clearly as possible between skin and other lesions not caused by yaws and those yaws lesions which they may closely resemble. At all stages of a mass campaign for the eradication of yaws, the clinical diagnosis should be as accurate as circumstances permit. However, in view of the limited time available in the initial treatment surveys and of the simple training given to many of the field staff, a certain proportion of diagnoses—probably about 10 per cent—may be expected to be erroneous. Such errors are all the easier to make as the skin has a limited number of reaction patterns, so that similar lesions may result from different causes. In the later stages of an eradication campaign, the manifestations of yaws have largely disappeared as a result of mass treatment with penicillin. It is then that many lesions not due to yaws become prominent, and at this stage accuracy of diagnosis assumes particular importance. The lesions of yaws were fully illustrated in C. J. Hackett's *An International Nomenclature of Yaws Lesions*, published by the World Health Organization in 1957. A new monograph, written by the same author in collaboration with Dr. L. J. A. Loewenthal, is intended as a companion volume to the earlier publication, and was prepared in response to requests for an illustrated handbook which would assist field workers in making accurate diagnoses (World Health Organization. Monograph Series No. 45: *Differential Diagnosis of Yaws*. Pp. 88 (52 figures). (Geneva: World Health Organization; London: H.M. Stationery Office, 1960.) 10 Swiss francs; 17*s*. 6*d*.; 3.25 dollars.

Hearing in Cetaceans

The skull of the Cetacea differs widely from the usual mammalian pattern; the relative sizes and positions of the bones forming it are much modified, and in many species they show a high degree of asymmetry. A complicated system of air sinuses connected with the Eustacian tube is associated with extensive venous plexuses in the basicranial region, the tympano-periotic bones are dissociated from the skull, and the bones of the middle ear with the tympanic membrane are also highly modified. Such peculiar conditions have long attracted the attention of comparative anatomists, whose observations are scattered through the literature of cetology. A recent paper (Fraser, F. C., and Purves, P. E., "Hearing in Cetaceans", *Bull. Brit. Mus. (Nat. Hist.)*, **7**, No. 1; 1960) reviews the history of the subject, and gives detailed comparative descriptions of the anatomy of the cetacean head based on original dissections, injected preparations, and radiographs. The authors had access to a large amount of unique material and have brilliantly illuminated much that was previously obscure. They have not, however, confined themselves to descriptive anatomy, for they have devised and carried out numerous elegant experiments to ascertain the functions of the various anatomical structures in the physiology of hearing. They have been able to show that the generally accepted theory which claims the Cetacea hear by bone conduction is not only erroneous but also impossible, and that in all the cetaceans the sense of hearing is the most important of the special senses. These points and many others are lucidly described and discussed in this scholarly and well-written paper, which is illustrated with numerous excellent plates. It is by far the most important work on the anatomy and physiology of the Cetacea to appear since Scholander's classic paper of 1940.

Effects of Maleic Hydrazide on Rust Fungi

Some interesting differential effects of maleic hydrazide on the growth of leaf and stem rusts of wheat are reported by D. J. Samborski *et al.* (*Canad. J. Bot.*, **38**, 1; 1960). The effect of this substance was investigated, using intact plants supplied with maleic hydrazide through the roots, detached leaves floated on solutions of maleic hydrazide, and spores germinated on maleic hydrazide solutions in agar. In each instance the growth of leaf rust was inhibited at concentrations of maleic hydrazide which had no effect on the growth of stem rust. Some resistant wheat varieties became susceptible to rust after treatments with levels of maleic hydrazide which

were not inhibitory to rust development. In some experiments, leaf rust races reacted differentially to maleic hydrazide. The authors consider that both nutritional and inhibitory factors may be involved in resistance and host–pathogen specificity.

Tenth Pacific Science Congress

The tenth Pacific Science Congress is to be held at the University of Hawaii, Honolulu, during August 21–September 6, 1961. The Congress will be divided into nine Sections: Agricultural Sciences; Anthropology and Social Sciences; Biological Sciences; Conservation; Forestry; Geography; Geophysical Sciences; Public Health and Medical Sciences; Scientific Information. Each Section will include a number of divisions. Three special symposia are being organized: "Man's Place in the Island Ecosystem"; "Science Museums in the Pacific Area"; "Galapagos Islands: a Unique Area for Scientific Investigations". Further information can be obtained from the secretary-general, Mr. Harold J. Coolidge, Tenth Pacific Science Congress, Bishop Museum, Honolulu 17, Hawaii.

University News: London

Appointments are announced as follows: Dr. D. R. Cox, reader in statistics at Birkbeck College, to the University chair of statistics tenable at that College; Dr. E. F. Scowen, reader in medicine at St. Bartholomew's Hospital Medical College, to the University chair of medicine tenable at that College; Mr. Arthur Summerfield, lecturer in psychology at University College, to the chair of psychology tenable at Birkbeck College; Dr. Donald Rogers, senior lecturer in physics at University College, Cardiff, to the University readership in chemical crystallography tenable at the Imperial College of Science and Technology from October 1. Titles within the University of London have been conferred as follows: professor of mathematics, on Dr. K. F. Roth, in respect of his post at University College; reader in medicine, on Mr. P. H. Sanderson, in respect of his post at St. Mary's Hospital Medical School; professor emeritus of biochemistry, on Prof. W. Robson, on his retirement from the professorship of biochemistry at King's College; reader in mathematics, on Dr. F. A. E. Pirani, in respect of his post at King's College; reader in mathematics, on Dr. S. Raimes, in respect of his post at the Imperial College of Science and Technology. Dr. F. A. Goldsworthy was appointed to the readership in applied mathematics at Queen Mary College (see *Nature*, **189**, 22; 1961), but was unable to accept the appointment.

Announcements

The following awards have been made by the president and council of the Royal Astronomical Society: *Gold Medal*: Prof. Herman Zanstra, until recently professor of astronomy in the University of Amsterdam, for his work on gaseous nebulæ; *Eddington Medal*: Prof. Hans A. Bethe, professor of nuclear physics at Cornell University, for his outstanding identification of energy-generating processes in stars.

Mr. J. A. Chaldecott, deputy keeper in the Department of Physics, Science Museum, South Kensington, has been appointed keeper of the Science Library in succession to the late Mr. H. T. Pledge. Mr. G. W. B. Lacey, assistant keeper, has been appointed deputy keeper in the Department of Aeronautics.

Mr. M. A. L. Banks, a managing director of the British Petroleum Co., Ltd., has been appointed a member of the Advisory Council on Research and Development to the Ministry of Power. The Council, which advises the Minister on the scientific aspects of his statutory duties, was recently reconstituted and its terms of reference amended so as to emphasize that its advisory functions cover all aspects of research and development concerned with fuel and power from the laboratory to industrial application.

The Industrial Science Achievement Award of the American Association for the Advancement of Science has been awarded to the Bell Telephone Laboratories, Inc., for its achievements in the field of universal communication during the year 1960. Among the work mentioned was: long-distance communication by reflecting radio-signals from *Echo* 1, the world's first electronic telephone switching system, the optical maser and solid state materials.

Applications are invited by St. John's College, Cambridge, for the Kenneth Craik Research Award, which is available for the assistance of persons engaged in postgraduate research, preferably in physiological psychology. The value of the Award will be £450 a year. Applications should be sent to the Master, St. John's College, Cambridge, so as to reach him not later than April 1, 1961.

A new colour magazine, *Knowledge*, has appeared. It is intended, by an easy appeal, to give children a glimpse of "the strange variety of things that the world has to show", as the editorial states. There is a South American edition too, and similar editions will be forthcoming from other countries; a cultural exchange of articles is planned. The magazine costs 2*s*. and appears every Monday (Purnell and Sons, Ltd., 37 Hertford Street, London, W.1).

The Royal Society has available for loan to film societies, educational institutions, schools, etc., a 16-mm. sound film in colour which runs for about 40 min. entitled "South from Chiloé" at a nominal service charge of two guineas per showing. This film tells the story of the Society's expedition to Southern Chile during the period October 1958–February 1959 which went to study the flora and fauna of this little-known region of the world. Requests for hire should be addressed to the Assistant Secretary, Royal Society, Burlington House, Piccadilly, London, W.1.

The Society of Leather Trades' Chemists is organizing a symposium on "The Technology of Drying Fibrous Materials with Particular Reference to Leather" during March 23–24. The symposium will be held in the Physical Chemistry Department, University of Cambridge. Further information can be obtained from G. H. W. Humphreys, 3 The Grove, Radlett, Herts.

A symposium on "Microchemical Techniques" is being organized by the Metropolitan Microchemical Society under the sponsorship of the International Union of Pure and Applied Chemistry. The symposium will be held at the Pennsylvania State University during August 13–18. Further information can be obtained from Mr. Howard J. Francis, jun., c/o Pennsalt Chemicals Corporation, P.O. 4388, Philadelphia 18, Pennsylvania.

NEW RESEARCH LABORATORIES OF HILGER AND WATTS, LTD.

SINCE the Second World War, the idea conjured up by the expression 'scientific instrument' has changed. It is well known that electronics has invaded every field of measurement, including the optical field, but it is less realized that instruments have tended to become larger. They have done so not only because of the addition of electronic units but also because this in turn has made possible complexities that would previously not have been considered.

To take one example, the quality of steel during the War was controlled by using the large quartz spectrograph, the photographic plates exposed in which carried the spectra of some twenty samples together with calibration spectra. The blackness of the lines at the appropriate places was measured with a microphotometer, reading from a galvanometer scale. Nowadays, when a charge of 70 tons of steel may be prepared and poured in 12 min., the foreman must have the analysis of a sample in as few minutes as possible if he is to have time to take any necessary action to rectify the charge. The automatic spectrograph or 'polychromator' takes up three or four times the space of the equipment previously used, but it provides an analysis of as many as thirty elements in about 3 min. in a typical case. To determine the carbon, phosphorus and sulphur in a sample, instruments are made that use the vacuum ultra-violet region of the spectrum as well as the air-penetrating ultra-violet region.

This trend, as well as the rise in numbers of instruments required, has induced Messrs. Hilger and Watts, Ltd., to build a new research laboratory at Camden Town, London, N.W.1, as an extension of their headquarters building there. Since the comprehensive damage to the factory caused by a flying bomb in 1944, research on instruments for analytical and kindred purposes has been carried out in rooms spread over the factory and adjacent outbuildings. (This does not apply to the research on surveying, photogrammetric and engineers' measuring instruments being done at the firm's Camberwell factory.)

The use of the new building was inaugurated by Sir George Thomson on December 15. The ceremony took the form of visiting the laboratories, in which normal work was in progress, and a luncheon attended by some 150 guests. The guests were drawn from among university physical and chemical departments, medical and government laboratories, and the research laboratories of industry.

Sir George was introduced by the chairman of the Company, Mr. G. A. Whipple, who is the present master of the Company of Scientific Instrument Makers. Mr. Whipple referred to the growth of the firm, which now has more than 2,000 employees, an associated company in the United States, and branch offices in Canada and Western Germany. He thanked the architect (Mr. J. Francis Smith), the builders (Messrs. Mullen and Lumsden), and the quantity surveyor (Mr. D. T. C. Thompson).

Sir George then proposed the toast of the Company and the new laboratories. He spoke of the 'pure' research worker's debt to industry, in that the needs of industry for large and complex instruments, which had to be reliable, encouraged the scientific instrument firms, which in turn could provide better instruments for pure research. Hilger and Watts was such a firm: "Twyman proved to industry the value of spectroscopic analysis. The demand so created made expansion possible, and its latest stage we are inaugurating to-day. From this, we benefit by the increased scale of the firm and by the great improvement this has made possible in design, which has given this great firm the enormous prestige it now holds throughout the world and which we are happy to be here to-day to celebrate".

Dr. A. C. Menzies, the firm's director of research, said in his reply that he had been concerned in his

Fig. 1. New Research Laboratory of Hilger and Watts, Ltd.

life with the building of three laboratories. However, it was only with the third of them, this new laboratory at Camden Town, that he had had the pleasure of contributing little but the expression of his requirements. This was the result of having good colleagues. He had worked with Sir George Thomson during the War, and it was at Sir George's instance that he had come to Hilger and Watts to succeed Mr. Frank Twyman. Sir George had added with a smile that the job was an easy one, so Dr. Menzies had frequently overcome difficulties since then by reminding himself that they could not exist. When he started with the firm, he turned one of the smallest rooms in an outside building into a dark room; "it had the advantage that water was laid on already". Such conditions made him resolve to work for a satisfactory, attractive place where his colleagues could work comfortably and effectively. Now they had it.

After the luncheon, the guests toured the laboratories and saw research being undertaken into spectroscopic analysis by emission, X-ray diffraction and X-ray fluorescence; infra-red absorption; optical design; absorption spectroscopy; optical instruments for the control of chemical processes; electron-spin resonance spectrometry; and generators for arcs and sparks.

N. J. GOODMAN

SCIENTIFIC RESEARCH IN AUSTRALIA

THE twelfth annual report of the Commonwealth (of Australia) Scientific and Industrial Research Organization, covering the year ended June 30, 1960, departs considerably from the form of previous years*. To facilitate its presentation to Parliament early in the 1960 Budget sitting, the chapters describing detailed technical matters characterizing previous reports have been replaced by a brief account of the more important developments during the year, and the details are to be published separately as a research review. The bulk of the present report consists of lists of published papers, and the membership of the Advisory Council, State Committees and staff and finance.

Of the expenditure of £9,489,741, £8,862,160 was on normal research activities and £144,600 on grants to outside bodies. Among new arrangements with the universities are noted support of an investigation by the Department of Zoology, University of Melbourne, into the effects of chromosomal inversion on viability of grasshoppers; collaboration with the University of New South Wales in an investigation of tritium-labelling techniques; continuation of research at the Australian National University into aggregation and denaturation of protein; and an extended loan to the Electrical Engineering Department, University of Tasmania, of the differential analyser developed by the Mathematical Instruments Section. Construction of the giant radiotelescope at Parkes, New South Wales, for the Division of Radiophysics is expected to be complete early in 1961.

Among the more important developments of the year noted in the chapter "Progress in Research" are the solution of serious problems preventing the development by irrigation of large areas of potentially fertile but intractable soils in the Riverina by using low concentrations of gypsum in the irrigation water to make the surface clays permeable. A study of the characteristics of coats of cattle in the tropics showed that gain in weight can be predicted much more accurately from the type of coat than from actual records of past gain in weight. A new process by which cheese is matured in a plastic wrapping has been adapted for Australian conditions, and a new kind of anti-fungal compound, 'Pisatin', has been isolated from peas. A strain of cocksfoot grass, introduced from Brignolles in France, has proved outstandingly productive as a component of winter pastures near Canberra and has persisted well under heavy stocking. Up to 90 per cent control of rabbits has been achieved with sodium fluoroacetate using a suitable bait; but its effective use depends on intelligent application of accurate knowledge of feeding habits and behaviour of the rabbit. Striking increases in beef production have been obtained in grazing trials with a grass-legume mixture in native spear grass country near Gladstone, and further evidence has been obtained of the primary importance of nutritional factors in determining the mortality among new-born lambs. The compounds causing certain off-flavours in butter have been identified, and most of the conditions under which these flavours develop have been recognized. Research at Crookwell has shown that sulphur is an essential constituent of the soil organic matter, and that lack of sulphur often limits the rate of build-up of soil fertility under improved pastures.

The first commercial plant for the manufacture of fully mechanized Cheddar cheese has been installed and successfully operated, and a field experiment in North Queensland suggests that control of the cattle tick can be greatly improved both by pasture spelling and strategic dipping. Equipment has been designed to overcome the difficulty of measuring the temperature of biscuits in a long conveyor-type oven due to the very limited access to the interior of the oven, and the method for producing washable non-iron effects in wool fabrics has reached commercial application. Two new statistical techniques have been developed for accurate spatial prediction of rainfall.

Polyethylene box liners have been used to increase significantly the storage life of four main varieties of apples. A new pre-steaming procedure has been developed which is greatly improving the drying of refractory timbers with a saving of 20 per cent in the time of drying with some species. It has now been found that sugar-cane wax as it occurs on the cane consists chiefly of polymerized long-chain aldehydes, with lesser amounts of long-chain alcohols. A study has also been made of the waxes coating the tubercule and diphtheria bacteria.

Investigations of the hardening of brass have proved that alpha brass is 'ordered' after slow-cooling treatments, and that the degree of order can be considerably increased by isothermal annealing at low temperatures. X-ray methods have been further developed for the determination of the structures of large molecules, by applying a high-power X-ray generator and by collecting intensity data at low

* Commonwealth of Australia. Twelfth Annual Report of the Commonwealth Scientific and Industrial Research Organization for the year ending 30th June, 1960. Pp. ii + 129. (Melbourne: Commonwealth Scientific and Industrial Research Organization, 1960.)

temperatures. In extensive tests at Umberumberka (Broken Hill) and at Lake Corella reductions of as much as 50 per cent of the normal evaporation have been obtained in still conditions by dusting with solid hexadecanol, but when the wind velocity exceeds 5 m.p.h. the saving is very much less. The first model of the 'Evaporotron', an instrument designed to yield direct readings of evaporation from natural sources on the eddy-flux principle, has been completed. Fundamental study of the physics of wool has established the existence of a transition temperature above which irreversible change occurs if the wool fibre is strained, and also that fibres of animal tendon have a transition temperature only slightly above normal blood temperature. Investigations of the retarding of non-enzymic browning of stored food by addition of sulphur dioxide or bisulphite indicate that the bisulphites may act through oxidation of the carbonyl compounds found in the aldose-amine reactions preceding browning.

STRONTIUM-90 IN HUMAN DIET IN THE UNITED KINGDOM, 1959

A REPORT by the Agricultural Research Council contains the results for the second year of the survey of strontium-90 in human diet in the United Kingdom which was initiated by its Radiobiological Laboratory in 1958*. Two types of investigation are described: a country-wide survey, which enables the mean ratio of strontium-90 to calcium in the average diet of the population to be assessed, and local studies in areas where the quantities of strontium-90 in the diet are likely to exceed the average.

The general organization of the country-wide survey was similar to that in 1958, though some additional foods were examined. The major effort was devoted to milk; bulk samples were prepared for analysis from milk collected twice each month from some 200 depots which handled more than 40 per cent of Britain's total production. Potatoes, leaf vegetables, flour, cheese, eggs, proprietary cereal-based infant foods and tea were also examined. It has already been reported that the quantity of strontium-90 in milk rose appreciably in the early part of 1959 with the result that the mean value for the twelve months ending in the middle of the year was 40 per cent greater than it had been six months earlier. Afterwards, however, the level of strontium-90 in milk decreased and, in the latter part of the year, it was similar to those observed in 1958; thus, the mean value for the preceding twelve months changed little between June and December. The country-wide mean values at the end of June and December 1959 were 11·7 and 12·2 $\mu\mu$c./l. (9·6 and 9·8 $\mu\mu$c./gm. calcium), respectively.

It is estimated that the mean ratio of strontium-90 to calcium in the average diet of the whole population in the United Kingdom during 1959 was 9·0 $\mu\mu$c./gm. and that it did not exceed 15 $\mu\mu$c./gm. in the diet of any large section of the population. Because of the relatively high levels of contamination early in the year, these values are about 50 per cent higher than those estimated for 1958. The estimated level in the diet of the population as a whole, however, represents less than one-twentieth of the maximum permissible level recommended by the Medical Research Council.

During the year, investigations were intensified to identify localized areas where the combination of high rainfall and agricultural factors could lead to abnormally high levels of strontium-90 in human food. Thirteen individual farms or groups of small adjacent farms were examined in wet upland areas in England, Wales, Scotland and Northern Ireland. All these areas are small, and only a fraction of the food consumed in them is produced locally. The results of these studies, however, enable conclusions to be reached as to the hypothetical maximum levels of strontium-90 which could occur in the diet of any individual. If it is assumed that an individual could consume the most highly contaminated foods of different types which have been found in these investigations (and these were, in fact, produced in widely separated parts of the country), the ratio of strontium-90 to calcium in the total diet would be 80 $\mu\mu$c./gm. This value, which is one-tenth of the maximum permissible level recommended by the Medical Research Council for individuals, is in fact considerably in excess of the likely levels in the diet of any one person. Moreover, it is less than one-third of the maximum permissible level for the whole population.

Milk continues to be the component of diet which contributes the largest quantities of strontium-90. The ratio of strontium-90 to calcium in milk is, however, similar to, or less than, that in many other foods. Since the concentration of strontium-90 in newly formed human bone depends on the ratio of strontium-90 to calcium, rather than on the absolute quantity of strontium-90 in the total diet, milk should not be regarded as giving rise to any special hazard.

Variations in the composition of diet usually have only small effects on the mean ratio of strontium-90 to calcium in the total daily intake. The only substitution in a normal diet which is likely to have a significant effect is that of wholemeal bread for white bread. The calculations in this report for the average mixed diet are for that containing white bread. The substitution of wholemeal bread which contains a higher quantity of strontium-90, and does not generally contain added calcium of mineral origin, would not, however, increase the ratio of strontium-90 to calcium in the average mixed diet by more than 6 $\mu\mu$c./gm. This increase is less than one-fortieth of the maximum permissible level for the general population.

Because climatic factors can exert considerable effects on the quantities of strontium-90 and of calcium which are absorbed by plants, and hence on the levels in human diet, it is not possible to make quantitative predictions as to the situation in the immediate future. There is, however, considerable evidence that strontium-90 which has hitherto been released into the atmosphere has already exerted its major effect; decreasing levels in human diet may therefore be expected in the future.

* Agricultural Research Council. Radiobiology Laboratory. Report No. 3.: Strontium-90 in Human Diet in the United Kingdom, 1959. Pp. x + 58. (London: H.M. Stationery Office, 1960.) 3*s.* 6*d.*

RESEARCH IN PARASITOLOGY

THE autumn meeting of the Parasitology Group of the Institute of Biology was held in the Zoology Department of Birkbeck College, London, on October 28. The meeting was very well attended and was devoted to five papers under the general title "Recent Advances in Fields of Parasitological Research". A short discussion followed each paper.

During the morning session the chair was taken by Dr. Ann Bishop. The first paper, given by Mr. Bernard Weitz (Lister Institute, Elstree), was on "Trypanosomiasis". Mr. Weitz pointed out that eradication of the disease depends on the control of the vector or the elimination of the reservoir hosts. *Glossina* can be controlled by bush clearing and, more recently, by the critical use of insecticides. Eradication of the insect by the sterilization of males by γ-irradiation is not practicable at present. Destruction of game removes the source of food of the vector and the parasite reservoir simultaneously. Consideration of the feeding habits of *Glossina* might permit the partial destruction of game, resulting in starvation of the fly. Animals which are frequently bitten by *Glossina* are usually tolerant to artificial infection, and, conversely, those which are infrequently fed on by the insect develop a parasitæmia and die more rapidly. On the other hand, it is difficult to understand how animals which are seldom or never bitten by tsetse become frequently infected unless by some other method of transmission. It is not clear whence the infection in the fly is derived. Immunity of animals can be assessed by a number of tests, but the specificity or sensitivity of the available serological techniques has led to confusing conclusions. The respiration test was recently used to measure the immune response of apparently resistant breeds of cattle. Recent attempts to investigate the antigenic pattern of trypanosomes showed that soluble antigens, released in the bloodstream of infected laboratory animals, influence infection. Laboratory animals immunized with these soluble antigens are protected against infection. Other antigens are released on mechanical disintegration of the trypanosomes. The occurrence of these antigens has been confirmed in the natural disease. Drugs are an important means of control of the disease but cannot be considered as a permanent measure. The local eradication of the disease must depend on concerted action by the use of all available methods of control.

This was followed by a paper by Dr. B. A. Newton (Department of Biochemistry, Cambridge) on "The Mode of Action of Quaternary Ammonium Trypanocides". The early work of Lock (1950) and Ormerod (1951, 1952) on the mode of action of ethidium bromide and 'Antryeide' indicated that these compounds differed markedly from the older type of trypanocidal drug (for example, trivalent phenyl arsenoxides, stilbamidine and acriflavine). Cytochemical studies led Ormerod to suggest that both compounds act in a similar manner by combining with, and inactivating, cytoplasmic ribonucleoprotein. Stimulated by these observations, work has been carried out on the action of ethidium bromide and 'Antryeide' on the trypanosomid flagellate, *Strigomonas oncopelti*, growing in a chemically defined medium. It has been found that these two drugs differ in their effect on the growth of *Strigomonas*; ethidium inhibits growth after about one generation, whereas 'Antryeide' changes the pattern of growth from a logarithmic form to a linear form. Examination of drug-treated cells has revealed an abnormal ratio of ribonucleic acid to deoxyribonucleic acid following ethidium treatment; no such change was observed after 'Antryeide' treatment. A more detailed investigation of the effects of these two compounds has shown that ethidium rapidly inhibits the synthesis of deoxyribonucleic acid, but permits the synthesis of ribonucleic acid and protein to continue for a limited time; antryeide, on the other hand, specifically inhibits the incorporation of purines into nucleic acid, but does not inhibit the net synthesis of nucleic acid so long as the organisms are able to synthesize purines. This action of 'Antryeide' is associated with the pyrimidine portion of the molecule. Examination of an 'Antryeide'-resistant strain of *S. oncopelti*, which has been developed *in vitro*, suggests that resistance is not associated with a change in cell permeability, or with a change in the affinity of cytoplasmic nucleoprotein for the drug. The possible nature of resistance was briefly discussed.

The afternoon session, under the chairmanship of Dr. E. L. Taylor, opened with a paper by Dr. C. Ellenby (Department of Zoology, King's College, Newcastle) on "Plant Nematology". Dr. Ellenby confined his remarks almost entirely to the cyst-forming eelworms of the genera *Heterodera* and *Meloidogyne* and considered aspects related to secretions not only from the plants but also from the nematodes themselves, and their influence on nematodes and plants respectively. Among the points mentioned were the secretions from bacteria and various host and non-host plants, the suppressant effect on eelworm populations of diffusates from the roots of marigold (*Tagetes*), hatching factors (including his own work and that of Schreiber), and the influence of nematodes on plant growth, trap formation in fungi and gall formation in the host plants. Gall formation and specificity were then outlined and this led to a consideration of 'resistance'. Finally, sex ratio and sex determination were discussed in the light of recent work on the possibility of sex reversal in a species of *Meloidogyne*.

The second paper was given by Dr. C. A. Wright (British Museum, Natural History) under the title "Malacology". Development of recent work on the identity of intermediate hosts of trematodes of medical and veterinary importance has shown the existence of a greater degree of host restriction at the molluscan stage of the life-cycle than was formerly accepted. This has led to the idea of a parallel evolution between trematode species and their molluscan hosts, and has emphasized the importance of infra-specific taxonomy, often at the population-level, in the study of the hosts. Originally the taxonomy of molluscs was based on shell characters alone, characters which are now known to be very variable, and the result was the naming of large numbers of redundant 'species'. Later workers used the radulæ of gastropods as a further aid to identification, but, here again, insufficient attention was given to individual variations. The study of anatomical characters, particularly of the genital system, has

been developed relatively recently and, in many cases, has provided useful taxonomic information. However, the plasticity of muscular structures and the effects on them of different methods of fixation, and also differences due to the maturity of the animal, necessitate a very careful interpretation of these anatomical data. Work is at present directed towards attempts to supplement the morphological criteria for species discrimination by biochemical characters, and the application of techniques such as paper chromatography of mucus, electrophoresis of blood proteins and systematic serology based on tissue extracts is beginning to provide a sounder basis for the systematics of the molluscan intermediate hosts of trematodes.

The last paper of the meeting was by Dr. C. Horton-Smith (Houghton Poultry Research Station) and was on "Poultry Parasites and their Control". A short review of the Coccidia of poultry introduced the main theme of the paper which was a discussion of the chemotherapy of coccidiosis, and the problems of developing drug resistance in *Eimeria tenella*; this occurs when the organism is exposed, over extended periods, to low and therapeutic concentrations of anti-coccidial compounds. The reactions of different strains of the same species, as well as the differences in species response to the same drug, were considered. The mode of action of anti-coccidial drugs, including the potentiation of sulphonamides by pyrimethamine, and the effect of anti-coccidials on developing immunity were also discussed. The selective action of certain sulphonamides on schizogony and, in particular, the second generation, associates this stage with the major role in the stimulation of resistance to *E. tenella*. This is amplified by the results of recent work. Finally, the mechanism of response to *E. tenella* was considered. Precipitating antibodies have been demonstrated as a result of the oral administration of oocysts, but the significance of these precipitins is, as yet, unknown.

The proceedings of this meeting will not be published in full.

SHEILA WILLMOTT

NATURAL RUBBER RESEARCH

THE Natural Rubber Research Conference, held in Kuala Lumpur during September 26–October 1, was sponsored by the Rubber Research Institute of Malaya and the Government of the Federation of Malaya. More than 280 scientists from 24 countries and all five continents attended, and considered some 76 research papers, making this by far the largest gathering ever to discuss research on the production and utilization of natural rubber.

As in the case of other industries based on natural products, the range of research sponsored by the natural rubber industry is exceedingly wide, and the papers were representative of many scientific disciplines. Thus, the topics discussed ranged from the role of trace elements in the nutrition of the *Hevea* tree, to biochemical and biophysical investigations of latex, and to the design of rubber components in structural engineering.

During the week, the conference heard lectures from three distinguished guests: Prof. G. E. Blackman, Prof. James Bonner and Prof. G. Gee.

Biological Studies of the Rubber Tree

Prof. Blackman spoke on "The Stimulation of Latex-Flow by Plant-growth Regulators". In tracing the history of the development of successful yield stimulant mixtures, which increase the flow of latex after tapping, he showed how this had been dependent on fundamental research into the activities of plant-growth substances. It had been estimated that several million pounds worth of additional rubber had been produced in Malaya during the past four years by the use of these stimulants. Prof. Blackman made it clear that there was still much to be learnt about the exact mechanism of the yield stimulation process; but, as other papers presented to the conference indicated, this is the subject of active work. Other authors discussed such matters as the formulation of stimulant mixtures, their application to the tree and factors influencing the response obtained. A new aspect of yield stimulation was provided by a report that yield increases may also be obtained by the use of antibiotic treatments.

Of no less importance than yield stimulation is the development of intensive tapping methods which permit the maximum exploitation of older trees. Experiments are now in progress to determine the optimum combinations of tapping systems and yield stimulation techniques to give the highest possible yield throughout the life of the rubber tree.

Several papers considered various aspects of the breeding and selection work which has always found a prominent place in the programmes of rubber research organizations. The newer varieties now being planted are capable of giving at least four times the yield of the unselected material used in the early years of the century. It is believed, however, that all the high-yielding Eastern varieties are susceptible to the South American leaf blight disease caused by the fungus *Dothidella ulei*. A number of speakers directed attention to the potential threat of this disease to the rubber-growing areas of Africa and Asia, and called for closer international co-operation in the development of high-yielding resistant varieties.

In the absence of any suitable method of true vegetative propagation, *Hevea* clones are still multiplied by bud-grafting on to seedling rootstocks. A procedure was described for bud-grafting seedlings considerably younger than those used at present, and an account was given of the successful rooting, under a mist spray, of leafy cuttings of a number of important *Hevea* clones. The commercial value of these new techniques remains to be evaluated, but the rooted cuttings are already providing an important source of uniform material for experiments, such as those on stock–scion effects. Meanwhile, techniques of growth analysis have been developed to give a clearer picture of the effects of rootstocks on scion growth and the variation in the pattern of growth in different clones.

In rubber, as in other crops, the standard method of deciding fertilizer requirements has always been by long-term field experiments. It now appears that leaf and latex analysis may offer an important complementary method. This work, pioneered in Vietnam, is now being vigorously pursued elsewhere.

As deficiencies in the major elements are corrected, more attention is being paid to the minor ones. It was emphasized that the applications of nitrogen, phosphorus and potassium so often used are in-

adequate on the generally poor soils of the humid tropics. Magnesium is as important as potassium, and deficiencies in several other elements are known to occur. These factors may greatly affect, and even invalidate, measurement of response to the three main elements.

The tree is now, more than ever, regarded as a part of a complex ecological system, and several papers described the marked effects of different cover species on tree growth. The beneficial effects of creeping legumes were particularly emphasized. Despite the large volume of present work on chemical weed control, there was only a single paper on this subject.

In the sessions on pests and diseases, interest centred on the root diseases, which can cause very serious losses to the rubber grower. One of the difficulties of the plant pathologist in this field was illustrated by a paper which showed that the usually accepted name for the pathogen of the common white root disease of *Hevea*, *Fomes lignosus*, was open to grave objection on taxonomic grounds. The potential hazards of the invasion of the cut surfaces of stumps by wind-borne spores, at the time of replanting, were emphasized, and it was shown that simple and inexpensive procedures could greatly reduce the toll of root disease in rubber plantings. Closely related to this problem is the study of factors affecting the rate of decay of rubber stumps and the role of biological agencies in the removal of this potential source of disease. The possible role of fungicides in the control of root disease was also discussed.

Fundamental work on the raw material of the natural rubber industry, *Hevea* latex, was well represented at the conference. Latex is very far from being a simple suspension of rubber particles in a watery medium. It contains a bewildering array of other particles which are under active investigation, in which use is made of the electron microscope, advanced forms of light microscopy and the ultracentrifuge. Workers in this field now appear to be agreed in regarding latex as a cytoplasmic fluid, and, as these studies develop, it will be interesting to see whether the particles which accompany the hydrocarbon in latex vessels have exact analogues among the known components of other plant cells, or whether they represent hitherto unknown entities.

It is now established that the process of rubber formation occurs within this complex system and it may be made to continue, experimentally, even after the latex has left the tree. An elegant account was presented of the way in which the acetate molecule is converted to rubber hydrocarbon in *Hevea* latex. Members of the conference also heard Prof. Bonner give a striking review of the whole process of rubber biosynthesis and set out suggestions for future research on the unsolved problems of the subject.

The biological complexity of latex is, of course, accompanied by a corresponding chemical diversity. The conference reviewed recent progress in the study of the many substances which accompany the rubber hydrocarbon. As with other fields of biological chemistry, these studies on the non-rubber constituents of latex have gathered momentum in recent years, with the development of new methods of chromatography and electrophoresis.

The biological character and diverse composition of natural latex render it highly susceptible to bacterial attack, and much time and effort have to be devoted to preventing the adverse technological effects which result. The subject is a complex one, and it gave rise to lively discussions during the conference. It appears to be agreed, however, that contamination of the latex begins within the cut ends of the latex vessels themselves and is reinforced at various stages in collection and processing. Measures to control it are already in widespread use and improvements are constantly being sought.

Chemistry and Technology of Rubber Preparation

Knowledge of the structure of the rubber molecule itself is still advancing, and new information is being obtained by the use of the electron microscope and light-scattering techniques. New data were also presented on the variety of reactions which the hydrocarbon can undergo. This reactivity has been turned to advantage to produce modified rubbers, such as the graft polymers. On the other hand, it also leads to the troublesome spontaneous change in properties known as storage hardening. The conference heard an account of a successful method for the inhibition of storage hardening based on a new theory that this change is due to the presence of aldehyde groups.

The bulk of the industry's revenue is still earned by sheet, crepe and other forms of dry rubber. Investigations were reported which should help the producer to avoid defects which down-grade his rubber when it is judged by the almost universal method of visual classification. There were also reports of work aimed at preparing dry rubber in novel forms which would be graded by technological properties rather than by appearance.

Concerning special dry rubbers, the conference heard of the increased interest in 'superior processing' rubbers, which have greatly improved extrusion characteristics. Several papers showed that new advantages and uses are being found and that, with this spur, new low-cost methods of imparting superior processing properties are being discovered. None of the rubbers produced by these alternative techniques possesses the all-round advantages of standard superior processing rubber, but they show promise for applications where the use of the standard product would be uneconomic.

Research and development are encouraging new applications of rubber in many fields. In the textile industry, natural rubber latex is now being used increasingly in the manufacture of non-woven fabrics and in carpet backings. New design methods are enabling engineers to employ rubber components with the same degree of confidence as those of the older structural materials. Further work is also giving road engineers a more detailed picture of the practical benefits to be gained by incorporating various types of rubber into bituminous road-binders.

Testing methods for quality and processability of latex concentrate were described, together with clonal influences on latex foam properties. On the subject of skim rubber, the by-product of the latex concentrate factory, the conference heard how processing methods could affect its properties. Methods for the treatment and utilization of factory effluents were also discussed.

Finally, in his address, "New Methods of Elastomer Synthesis and their Impact on Natural Rubber", Prof. Gee brought into the open the question that had formed the background to many of the discussions during the week: "Can natural rubber, even

when produced by the most economical means, meet the challenge of the new synthetics?" Prof. Geo's answer was "Yes", provided the natural rubber industry continued and intensified its fundamental research and technical development in the right directions. He showed that no single elastomer is supreme in all respects and that each of them, including natural rubber, can hold its place in the expanding market. He also described the striking results which may be obtained by blending natural and synthetic rubbers and how the presence of the reactive groups influences this blending.

There can be little doubt as to the success of the conference in bringing current ideas on natural rubber research into sharper focus and in stimulating new approaches to the many problems raised. The proceedings of the conference are to be published early in 1961, and those wishing to obtain copies should write to the Director, Rubber Research Institute of Malaya, P.O. Box 150, Kuala Lumpur, Malaya.

S. G. Boatman
J. Bolton
R. S. Gale
G. F. J. Moir

ELEVENTH GENERAL CONFERENCE OF WEIGHTS AND MEASURES

THE eleventh General Conference of Weights and Measures was held in Paris during October 11–20 under the chairmanship of M. Barrillon, president of the Academy of Sciences. Thirty-two States were represented at the Conference, which was held at 19 Avenue Kléber, in the former Hotel Majestic now taken over by the Ministère des Affaires Étrangères for use partly as offices and partly as a meeting place for national and international conferences. One epoch-making scientific decision was taken, namely, to re-define the metre in terms of a natural atomic standard, the wave-length of light, thus deposing the platinum–iridium metre bar—the International Prototype Metre—from the supremacy it has held in the field of length measurements since 1889. Three very important administrative and financial resolutions were passed which are crucial to the future development and efficiency of the weights and measures organization. Before dealing with these and other decisions and with an unfinished effort of the Conference to modernize the international treaty on which its authority is founded, it would be well to give a brief outline of the history and development of the whole organization.

International co-operation in scientific metrology depends on the Convention du Mètre, a treaty signed in Paris by the plenipotentiaries of seventeen sovereign States on May 20, 1875. An agreement was thereby made to establish and maintain, at joint expense, a central laboratory and office, known as the Bureau International des Poids et Mesures, with the primary duties of maintaining, improving and extending the use of the metric system. The treaty organization, which the United Kingdom joined in 1884, now represents thirty-eight States (Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Chile, Czechoslovakia, Denmark, Dominican Republic, Finland, France, Germany, Hungary, India, Indonesia, Ireland, Italy, Japan, Korea, Mexico, Netherlands, Norway, Poland, Portugal, Rumania, Spain, Sweden, Switzerland, Thailand, Turkey, the United Kingdom, the United States, Uruguay, the U.S.S.R., Venezuela and Yugoslavia (Indonesia and Venezuela joined after October 1960). It acts under the authority of the General Conference of Weights and Measures, constituted by delegations nominated by the Governments of the member-States meeting every six years, with the aid of the International Committee of Weights and Measures—an elected executive body of eighteen members (each from a different State) meeting every two years. This Committee administers the scientific and financial affairs of the Bureau International in between general conferences, drafts recommendations relating to units and standards of measurement with the help now of six expert advisory committees and acts as a steering agency during General Conferences.

The Convention was revised on October 6, 1921, mainly to extend the work of the Bureau International des Poids et Mesures to the standards of electricity and photometry. Up to that date the Bureau International, as custodian of the International Prototypes of the Metre and Kilogramme, was chiefly concerned in its laboratory work with the maintenance, by means of periodical comparisons, of the various national copies of these prototypes issued to the member-States in 1889 and afterwards. The derived standards of volume (or capacity), density and atmospheric pressure naturally came within the responsibilities of the Bureau International; and, as the length of a material standard is dependent on its temperature, a practical scale of temperature was maintained. As a consequence of the 1921 revision, high-class electrical and photometric equipment was installed at the Bureau International for periodic intercomparisons of groups of standard resistors, standard Weston cells and standard lamps sent in by the national laboratories. In this way, just as for the national metres and kilogrammes, the uniformity of the electrical and photometric standards maintained by the various countries is readily checked, and any individual divergences from the general average which are unusual are identified and reported.

During recent years the rapid development of applications of radioactivity and the ionizing radiations in the scientific, medical and technological fields has created an urgent need for a central standards laboratory to work on the basic metrology of ionizing radiations and to correlate the standards and measuring techniques developed in the national and other specialized laboratories. In 1958 the International Committee established its expert advisory committee for the ionizing radiations which has produced proposals for a new Bureau International des Poids et Mesures laboratory and equipment, together with a general plan of the work to be done and the staff required. Recommendations embodying these proposals were submitted to the eleventh General Conference by the International

Committee, with others for: (1) increasing the staff and modernizing the equipment in existing sections of the Bureau International; (2) changing the rule by which the total annual subvention for maintenance of the Bureau International is apportioned among the member-States. All these recommendations were unanimously adopted and the Conference thereby sanctioned:

(*a*) The creation of a new section at the Bureau International des Poids et Mesures for work on the basic metrology of the ionizing radiations, the construction of a laboratory and the purchase of equipment at an overall cost not exceeding 1,800,000 gold francs (about £210,000).

(*b*) The raising of the total annual subvention made jointly by the member-States from the present figure of about 400,000 gold francs (£47,000) to 900,000 gold francs (about £105,000).

The intentions of these decisions are that the Bureau International, which has hitherto had to work within limits imposed by a much too narrowly restricted budget, should be better able to fulfil its function as a supra-national standards laboratory and to provide it with reasonable funds for this purpose.

To enable the Bureau International to initiate as early as possible the new section on the ionizing radiations, the Ford Foundation has made a grant of 32,500 dollars to cover the period intervening until the new funds voted by the Conference become payable by the member-States on January 1, 1962. The National Research Council of Canada has temporarily seconded to the Bureau International Dr. C. Garrett, head of the Ionizing-Radiations Section of its Division of Applied Physics, who will take charge of the new section during this same period. His duties will include detailed planning of the ionizing-radiations laboratory and the ordering of its equipment; he will also advise the director of the Bureau International des Poids et Mesures on the selection and appointment of staff for the new section.

Despite its partial revision in 1921, the Convention du Mètre retains many clauses, suited both scientifically and politically to nineteenth-century circumstances, which tend to hinder adaptation of the organization to the rapidly changing and complex needs of scientific metrology and international relationships in the twentieth century. Accordingly, a special commission of the International Committee had been working on the draft of a revised treaty since the last Conference in 1954 and this draft had been sent to Governments for comment some months ago. The scientific clauses were easy to settle, but it was soon realized during the eleventh Conference that there was no hope of securing immediate and unanimous approval of the political and administrative clauses of a modernized treaty by the various delegations, so the matter was left to proceed by negotiation through diplomatic channels.

The fundamental scientific resolution unanimously adopted by the Conference re-defined the metre as equal to 1,650,763·73 vacuum wave-lengths of the orange line (6058 Å., spectroscopic designation $2p_{10}$–$5d_5$) emitted by the krypton atom of mass 86. The source of this radiation, recommended in October 1960 by the International Committee, is an Engelhard type of krypton-86 hot-cathode discharge lamp[1,2] enclosed in a cryostat maintained at the triple-point of nitrogen (about 63° K.). The specification of the conditions of excitation and observation ensures a reproducibility of the new optical metre to about 1 part in 100 millions, and there are good expectations of improving on this very soon. Recent experimental work at the National Research Council (Ottawa) and the National Bureau of Standards (Washington) indicates that continuity of the unit metre distance is maintained to the accuracy with which it was represented by the separation, at 0° C., of two parallel defining lines engraved on the prototype platinum–iridium bar, namely, 1 part in 4 millions. Moreover, according to the new definition, the angstrom unit (Å.) becomes equal to 10^{-10} metre exactly[3].

It is interesting to digress here by noting that the Weights and Measures Bill now before Parliament proposes to define the yard as equal to 0·9144 metre exactly. The same value has already been adopted by the National Physical Laboratory (and five other national laboratories) for non-metric measurements of length in science and technology[4]. If the Bill is enacted, the yard for all purposes in Britain will therefore be effectively based on the new primary wave-length standard through the adopted relationship with the metre.

Among other scientific resolutions adopted by the Conference are the following relating to units and standards of measurement:

(1) Ratification of the improved astronomical second of time[5], with a rider urging standards and other laboratories to proceed as actively as possible with the work to establish a second based on an atomic frequency standard.

(2) Provisional retention of the Potsdam gravimetric system[6] for use in physics until the results of certain absolute determinations of gravity now in progress are made known.

(3) Approval of a detailed list of the international system of units[7] (designation *SI*) founded on six basic units (metre, kilogram, second, ampere, degree Kelvin and candela).

(4) Approval of a new draft of the International Temperature Scale (1948)[8], henceforth to be known as the International Practical Scale of Temperature (1948).

(5) Inviting the International Committee to study, and if possible resolve, the confusing situation due to the difference of 28 parts in a million between the cubic decimetre and the litre[9].

The eleventh General Conference was by far the most interesting and stimulating of the three Conferences held since the end of the Second World War. Besides giving official recognition to a fundamental change in the definition of the metre, some very difficult administrative and financial questions were resolved in such a way as should engender a new look for international scientific metrology during the next decade.

This article is published by permission of the director of the National Physical Laboratory, who led the United Kingdom delegation at the eleventh General Conference.

H. Barrell

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[2] Engelhard, E., *P.V. Com. int. Poids Mes.*, **26**, B, Annexes *M2*, *M3*, *M4*, *M5*, *M6* and *M7* (1958).

[3] Barrell, H., *Nature*, **180**, 1387 (1957).

[4] *Nature*, **183**, 80 (1959).

[5] *P.V. Com. int. Poids Mes.*, **25**, 77 (1956).

[6] Kaye, G. W. C., and Laby, T. H., "Tables of Physical and Chemical Constants", twelfth ed., 17 (Longmans, 1960).

[7] *P.V. Com. int. Poids Mes.*, **25**, 117 (1956).

[8] *Trav. Bur. int. Poids Mes.* (9e Conférence Générale, 1948), **21**, 89 (1952).

[9] *P.V. Com. int. Poids Mes.*, **22**, 94 (1950).

DOMESTIC FOOD CONSUMPTION AND EXPENDITURE IN BRITAIN

THE recently issued annual report of the National Food Survey Committee for 1958 is the ninth in the series of surveys, begun in 1950, of food consumption and expenditure on food in private households in the United Kingdom*. During 1958, 8,611 records were compiled from 827 polling districts in England, Wales and Scotland. The survey methods remained unchanged. Information was collected on all foods purchased or brought into the household during one week, but, as before, soft drinks, sweets, ice-cream and snacks were not included, and full details of meals taken away from home not obtained; an allowance has been made for these when the nutritive value of the diet is assessed. Records are no longer sought of changes of larder stocks, these being largely unnecessary for the low-income groups in which daily shopping is traditional. In the higher-income groups bulk purchasing of some items is more frequent, and a large number of households would have to be surveyed to obtain a statistically correct record.

While the survey is thus incomplete on the food consumption side, it provides much valuable information on the expenditure on food and eating habits of the community, set out in a series of well-presented tables which enable the expenditure on many types of foods by families differing in social class, composition and location to be compared.

For Britain as a whole, weekly expenditure on food (with allowances for free and home-grown food) rose from 29*s*. 1*d*. per head per week in 1957 to 29*s*. 4*d*. in 1958. This small increase is attributed to higher seasonal prices. Since 1954, when rationing ceased, the percentage rise in expenditure on food has increased year by year. The report notes that "the average calorie intake of the population has reached such a level that there is little scope for increases in the quantum of purchases except through improvements in quality, service, processing and packing or through increased wastage".

Little change has occurred since 1954 in expenditure on the broad food groups, but within these groups there has been a significant increase in purchases of processed foods such as cakes and biscuits and certain kinds of processed meat, fish, vegetables and fruit. The consumption of butter continues to rise and that of margarine to fall. The steady decrease in expenditure on bread has halted and shows a slight rise, mainly due to the purchase of dearer types of bread.

On the average there has been little change in the nutritive value of the average British diet since 1954. When compared with the allowances recommended by the British Medical Association, it is found to be satisfactory. Supplies of nearly all the nutrients are, however, greater in the higher- than in the lower-income groups. In the latter, supplies of protein are lower than the British Medical Association's recommended allowance for households, with total incomes of less than 230*s*. a week, and old-age pensioners may be somewhat short of iron. No data are available indicating that these deficiencies affect the health of the groups in question.

A chapter on geographical differences in food purchasing contains some interesting information. For example, in Scotland expenditure on cakes and biscuits was 36 per cent more than the average, and that on flour 40 per cent less than the average. Welsh households spent 30 per cent more than the average on flour, 60 per cent more on butter and 12 per cent less on cakes and biscuits.

Two new special studies were included in the 1958 survey. One deals with the effect on the household diet of the housewife's employment, which causes a change in the whole pattern of eating habits with more meals and snacks taken away from home. The results of this study were inconclusive, because of the difficulty in obtaining information about outside meals, and elaborate statistical treatment was scarcely warranted. The second special study was concerned with the food consumption of households dependent on one woman with no other wage-earner, and here the information collected was disturbing. The diets were in general less than the average in nutritive value, particularly in protein and calcium content, and, in the larger families so dependent, there was also a deficiency in calcium and riboflavin.

While the picture is on the whole satisfactory, the data for larger families check complacency. In households of two adults and two or more children, protein supplies are less than the British Medical Association's recommended allowances, and when there are four or more children the diet falls short of the allowance not only with respect to protein but also in calorie value and calcium and riboflavin content. The fact that these figures are an average for large families of all income groups means that consumption in the lower-income groups in this category is far less than the average for the whole groups of households surveyed. JOYCE DOUGHTY

* Ministry of Agriculture, Fisheries and Food. Domestic Food Consumption and Expenditure, 1958: Annual Report of the National Food Survey Committee. Pp. vii + 185. (London: H.M. Stationery Office, 1960.) 10*s*. net.

IMMUNIZATION IN INDIA

IN a recent issue of the *WHO Chronicle* the possible part that could be played by wide-scale immunization against disease in India, provided outside support is given, is considered (**14**, No. 11; November 1960).

About 13·5 per cent of India's 408 million inhabitants are infants and children of 4 and under; about 25 per cent are between 5 and 15 years old. Diphtheria, whooping cough and tetanus cause widespread morbidity and mortality in these age groups. Diphtheria—also rife in rural areas—is responsible for between 2,000 and 5,000 admissions every year to hospitals in cities such as Calcutta and Bombay, and no fewer than 84 per cent of the cases are children between 2 and 10 years of age, while 11 per cent are infants. Investigations have shown that

tetanus (including that of the new-born) is an important cause of death in rural India. Whooping cough not only causes much suffering but also many deaths from secondary complications.

In 1959, the twelfth session of the World Health Organization Regional Committee for South-East Asia recommended the routine vaccination of children against all three diseases. The major obstacle to this course in India has hitherto been the difficulty of obtaining the necessary vaccines; local production is inadequate and the cost of importing them prohibitive. It has therefore been decided to expand their local manufacture with help from the World Health Organization and Unicef as a preliminary to a country-wide immunization campaign against these three diseases.

A pilot unit for the production of the vaccines will be set up at the Central Research Institute, Kausali. As soon as practical methods of preparation have been worked out, standardized and tested, other laboratories will be encouraged to adopt the approved methods and start production so that the entire needs of the country can be met step by step. At the same time, epidemiological information on the diseases will be collected from both rural and urban areas and used to plan a practical and economical immunization programme for the whole country. The vaccines will be manufactured at Kausali in accordance with procedures recommended by the World Health Organization, and a consultant from that Organization will be assigned to the project. Equipment, apart from that already available in the country, will be supplied by Unicef.

Two workers from the Kausali Institute are at present in Australia studying vaccine production and immunology, including the production of triple vaccine against diphtheria, whooping cough and tetanus. On their return to India they will work with the staff of the special vaccine production unit. Another worker from the Institute will be trained overseas at a later date. It is expected that the Institute will be able to produce 4,000,000 ml. of vaccine a year to begin with, and within three years will reach the target of 7,000,000 ml. a year.

DISTRIBUTION OF CERTAIN POPPY-FUMARIA ALKALOIDS AND A POSSIBLE LINK WITH THE INCIDENCE OF GLAUCOMA

By Drs. SOHRAB A. E. HAKIM, VALERIE MIJOVIĆ and JAMES WALKER
National Institute for Medical Research, Mill Hill, London, N.W.7

GLAUCOMA, suddenly affecting large numbers of people and associated with dropsy ('epidemic dropsy'), has occurred sporadically in India in epidemic form, and these epidemics were eventually traced[1] to the contamination of cooking oils with the seed-oil of the common prickly yellow poppy, *Argemone mexicana* L. Since epidemic glaucoma in India was caused by a plant poison, it was suggested[2] that endemic (primary) glaucoma of unknown aetiology, occurring in other parts of the world, might also result from some toxic cause. Endemic glaucoma, empirically recognized for centuries, is one of the major causes of blindness, and Duke-Elder[3–5] has repeatedly emphasized that, in spite of extensive researches, its basic cause, mechanism, and radical treatment remain unknown. Glaucoma is symptomless during the greater part of its relentless development, and in its early stages merely shows as an increase in the normal range of fluctuation in the fluid tension of the eye. Only later is the tension permanently raised, accompanied by progressive, perhaps independent, degeneration of the drainage mechanism and nervous structure of the eye[3,6,7]. In spite of facilities for early detection and medical and surgical treatment available in advanced countries, such as the United Kingdom, nearly 60 per cent of cases proceed to total blindness[8].

The seed-oil of *Argemone mexicana* contains the *iso*quinoline alkaloids sanguinarine and dihydrosanguinarine[9], and we[10a,b] have described elsewhere an investigation of the biological effects of argemone oil and of sanguinarine. In particular, the production of experimental glaucoma and dropsy was described, and both these cardinal signs of the human epidemic disease were reproduced in animals for the first time. Sanguinarine, a pure alkaloid, was thus the first known naturally occurring substance successfully used as a tool for the production and study of experimental glaucoma. Eye-tension-raising properties were, however, not restricted to sanguinarine and to argemone oil. Tests on a large group of rabbits established that the closely related alkaloid chelerythrine, and oils or watery extracts of seven other species of poppies also raised eye tension[10]. These observations of ours led others[11] to investigate in rabbits the effects on eye tension of a number of *iso*quinoline alkaloids belonging to various types; besides sanguinarine, the intravenous injection of codeine, papaverine, narcotine, bulbocapnine, corydine, corybulbine, and chelidonine also produced acute rise of eye tension[11]. Our own experiments were continued[12] in India with rhesus monkeys, as their eyes more closely resemble those of man. Repeated injections of sanguinarine produced dropsy and sustained rise in eye tension, while feeding with argemone leaves, or with seed-oil of either argemone or the Indian fumitory (*Fumaria indica* Pugsl.), produced dropsy and a smaller rise in eye tension.

Sanguinarine is a member of the small benzophenanthridine group of *iso*quinoline alkaloids. Although isolated[13] in 1829 from *Sanguinaria canadensis* L., it had, up to the time the present work was begun in September 1956, been detected in only nine species of poppy-fumaria weeds [*Argemone mexicana* L.; *Bocconia pearcei* Hutchinson; *Chelidonium majus* L.; *Dicranostigma franchetianum* Hook. f. et Thoms.; *Eschscholtzia californica* Cham.; *Glaucium flavum* Crantz. (= *G. luteum* Scop.); *G. fimbrilligerum* Boiss.; *Macleaya microcarpa* Fedde (= *Bocconia microcarpa* Maxim.); *Sanguinaria canadensis* L.], while its occurrence in three other species (*Bocconia cordata* Willd.; *Dicentra spectabilis* L.; *Stylophorum diphyllum* Nutt.) was not confirmed[14,15]. While our work was in progress, its presence in *Glaucium corniculatum* Curt. was recorded by Slavík and Slavíková[16], and, since our work was completed in March 1958, the pains-

taking researches of Slavík and his collaborators have demonstrated its presence in *Dicranostigma franchetianum* Fedde[17], *Dicentra spectabilis* L.[18], *Glaucium flavum* var. *fulvum* Fedde[19], *G. vitellinum* Boiss. et Buhse[20], *G. elegans* Fisch. et Mey.[21], *Argemone alba* Lestib.[22], *Meconopsis aculeata* Royle, *M. rudis* Prain, *M. paniculata* Prain, *M. betonicifolia* Franch., *M. horridula* Hook. f. et Thoms., and *M. latifolia* Prain[23]; a few of these observations confirm, and they are in general complementary to, those recorded in the present article.

The meagre information hitherto available on the distribution of sanguinarine may be attributable to difficulties in adequate extraction and identification, since sanguinarine and some of the other alkaloids with which we are concerned show somewhat unusual partition properties and are not detected by several of the common 'general' reagents for alkaloids. Fortunately, these alkaloids fluoresce brilliantly in distinctive colours in filtered ultra-violet light, and the fluorescences show individual and characteristic changes in colour with change of *p*H. They could be separated either by paper chromatography or by paper electrophoresis and detected even in exceedingly small quantities by their fluorescences, R_F values, and relative speeds of migration. Paper chromatographic runs were made by descending flow on Whatman No. 1 paper using *n*-butanol/glacial acetic acid/water (63 : 10 : 27 or 100 : 10 : 30); second dimensional runs were made with a similar mixture (85 : 1 : 14)[24]. In filtered ultra-violet light, sanguinarine spots fluoresced with a bright orange colour, chelerythrine and coptisine spots with a golden yellow colour, and berberine spots with a brilliant yellow-green colour; touching the spots on the paper with a glass rod previously dipped into *N* sodium hydroxide produced characteristic reversible changes in fluorescence. Paper electrophoresis runs were made on Whatman No. 54 strips, 12·5 cm. wide, moistened with 10 per cent formic acid[25], with a potential difference of 1,000 V. and a potential gradient of 20 V./cm., using sanguinarine, or berberine, as marker.

Herbs of the families Papaveraceae and Fumariaceae were gathered from the Royal Botanic Gardens, Kew, the University Physic Garden, Oxford, and from India. Different parts of each plant were ground in small volumes of glacial acetic acid, which was found to be the best extraction medium. The alkaloids in such extracts were easily and clearly separated by paper chromatography and paper electrophoresis[10c]. From a few drops of plant extract, ten or more fluorescent spots were frequently obtained by either method. Chromatographically separated fluorescent spots were eluted and re-spotted for electrophoresis for confirmation of their basic nature and identity. With these very sensitive methods, numerous fluorescent alkaloids were readily separated from even a few milligrams of plant material in suitable cases, and the results are recorded in Table 1 for the distribution of four of the principal alkaloids (berberine, coptisine, chelerythrine and sanguinarine) between the roots, stems, leaves, flowers, capsules, and seeds—or such of these parts as were available to us—of the species examined. Separation of alkaloids present in gram quantities of plant material could also be effected on small alumina columns developed with benzene, acetic acid and ethanol[24].

Sanguinarine was found in 49 out of the 53 available species of poppy-fumaria weeds and usually in several different morphological parts of the plant (Table 1). Far from being restricted to only a few genera of poppy-fumaria plants as previously believed[26], it was perhaps the commonest fluorescent alkaloid detected among these weeds. It was almost invariably found in the leaves and stem. When the same species was collected from different localities, or at different stages of its growth, small qualitative and quantitative variations were noted in the alkaloidal content. Chelerythrine was found less frequently than sanguinarine; it was common in certain genera and rare in others. Berberine, though of fairly frequent occurrence in poppy-fumaria plants, was restricted to certain genera with rare exceptions. Sanguinarine and chelerythrine were not detected in a few specimens from the phylogenetically related family Berberidaceae, in which berberine was abundant in the stems yet absent from the leaves. Canadine was rarely detected. On the other hand, the closely related protoberberine alkaloid coptisine was very often seen. The more widespread occurrences of sanguinarine and coptisine that have emerged from the present work are of great interest, but perhaps not altogether surprising, as protopine is said to be without doubt the most widespread of all alkaloids and to have been found in all papaveraceous plants which have been exhaustively examined[15,27], and sanguinarine, coptisine, and protopine probably share, according to widely accepted views on alkaloid biosynthesis[28,29], a common protoberberine precursor.

We have found sanguinarine in the root, stem and leaves of the 'opium' poppy (*Papaver somniferum* L.) but not in the capsule or in the seeds. It is presumably not present in opium as it has not been noticed in spite of intensive studies on the alkaloids of opium[27] during the past hundred years. In Persia young opium plants pulled up to prevent excessive cropping are used as pot herbs[30] and are fed to cattle. Although we failed to detect sanguinarine in the specimen of *P. somniferum* seeds examined, the culinary use of poppy seeds (maw seed, *P. somniferum* L. var. *nigrum* DC.) should be viewed with suspicion, as we examined a poppy-seed cake purchased in a London supermarket and found it to contain several fluorescent bases and a small but quite unmistakable proportion of sanguinarine. Poppy seeds and their oil are extensively used in bread and confectionery in France, south-east Europe, and western Asia, especially by Jews, who, as a people, have a notably high incidence of glaucoma[31,32]. Insidious sanguinarine poisoning could occur from various species of poppy seeds, especially those of *P. rhoeas* L., which have a tendency to adhere to cereals to the extent of up to 10 per cent. These seeds are also fed to poultry as 'tail-corn', and probably transmit their alkaloids to eggs. Through the courtesy of Dr. M. E. Langham and Dr. J. G. Dobbie of the Medical Research Council Ophthalmological Research Unit, Institute of Ophthalmology, we have been able to examine the eggs from hens forcibly fed with sanguinarine, using the hydrolytic-extractive procedure described in the following article; we found sanguinarine in the whites and traces in the yolks along with other fluorescent bases, none of which was found in control eggs.

Sanguinarine was found in nearly all the 53 species of poppy-fumaria weeds which we examined. These species are distributed among 14 genera, and this suggests that sanguinarine is probably present in many more of the 675 species[33] of this vast alkaloid-rich family with its world-wide distribution. In view

Table 1. Morphological Distribution of Four 6oQuinoline Alkaloids in 53 Species of Poppy-Fumaria Weeds

Plant	Berberine						Coptisine						Chelerythrine						Sanguinarine					
	r	*s*	*l*	*f*	*c*	*sd*	*r*	*s*	*l*	*f*	*c*	*sd*	*r*	*s*	*l*	*f*	*c*	*sd*	*r*	*s*	*l*	*f*	*c*	*sd*
Papaveraceae																								
Argemone alba Lestib.		+	+		+	+														?	–		+	–
A. grandiflora Sweet	?	–	–		+	+	+	+	+	–	+	–	+	–						+	?		+	+
A. mexicana L. (London)		+	+		?	+		+	+		+	+		–				–	+	+	–	?	+	+
A. mexicana L. (Bombay)	+	–	+	?	+	+	–	–	–				+	–					+	+	?			
A. mexicana L. (Bombay seedlings)	+	–	–				–						?	?										
A. mexicana var. *ochroleuca* (Sweet) Lindl.		+	+		+	+			+	–	+	+								–	–		+	+
A. platyceras Link et Otto		–	–		+	–			+	–	+	+		*						+	–		+	+
A. platyceras var. *rosea* Coult.		+			+	+			+	+	+	+		–				–		–	?		+	+
Chelidonium majus L.	+	+	–		+	+	+	+	+		+	+	+	+				–	+	–	?		+	?
Dicranostigma franchetianum Fedde	–	–			–		+	+	+		–		+	?	+				–	+	+		+	
D. lactucoides Hook. f. et Thoms.						–		+	+		–				+		–				+		+	+
Eschscholtzia caespitosa Benth.		–				–			+	–		+		+				+			+			+
E. californica Cham. (London)	–	–				–	+	+	+			?	+	–	+			+	+	–	+			+
E. californica Cham. (N. India)	–	–				–	–	–	?				+	–	+				+	–	+		+	?
E. californica var. *alba* Fedde		–				–					+	?												
E. lobbii Greene	–	?				–	+		–			+	+						+	?	+		+	+
Glaucium corniculatum var. *rubrum* S.M.						–		+	+		+			+	–						+			?
G. flavum Crantz						–		–	–											?	+			+
Hypecoum grandiflorum Benth.						–															+		+	+
Macleaya cordata R.Br.	–					–	+								+	–					+			
M. microcarpa Fedde						–		+	–												+			
Meconopsis betonicifolia Franch.																					+			
M. cambrica Vig.		–																		?	+			
M. cambrica var. *aurantica*		–							+											+	+			
M. dhwojii G. Taylor		–																		+	+			
Papaver aculeatum Thunb.	–					–			?										+					
P. atlanticum Ball	–					–			+		?	–							?		+			
P. commutatum Fisch. et Mey.		–	?			–				–	?	?				?			?		+			
P. dubium L.	+	+	+		+	–	+	+	+			+											+	–
P. glaucum Boiss. et Hausskn.					–	–					+												+	
P. heldreichii Boiss.					–						?					?								
P. hybridum L.	+	–	+	+		–	+	+	+	+		+							+		?	?		
P. monanthum Trautv.						–			–		+								+	?	–		+	–
P. nudicaule L.						–	+	–	–	+	?	–							+	–	–		+	–
P. orientale L. (Oxford)						–	–	–	–		–	–								–	–		–	–
P. orientale L. (London)						–		+	–		+	–								–	–		–	–
P. paroninum Mey.						–		+			–	–							+	–	+		?	–
P. pilosum Sibth. et Sm.	–					–	+	+	+		–	–								+	+	–	+	–
P. rhoeas L. (N. England)								?	?	–	?	–		?		?			+	–	?	?	–	+
P. rhoeas L. (Oxford)	–					–	–	+	+	+	+	+								?	?	–	?	?
P. rhoeas L. (London)								+	+	–	+	+											?	–
P. setigerum DC.				–							+	?								+	+			
P. somniferum L. var. purple (Oxford)	–	–					+	–	+					?					+	+	+			
P. somniferum L. var. white (Oxford)	–					–	–	+	–										?	+	–	+		
P. somniferum L. var. red (N. India)							–	–	–	–										–				
P. somniferum L. var. red (Anatolia)								–	–			+							+	–	?			
P. triniifolium Boiss.							+	+	+		+													
Roemeria rhoeadiflora Boiss.							+	+	–		+													
Stylophorum diphyllum Nutt.								+	+					+						+	+[e]			
Fumariaceae																								
Corydalis chaerophylla DC.		?	–					+	+											+*	+*			
C. cheilanthifolia Hemsl.		+	–			+		+	+		+	+								+	+		+	?
C. glauca Pursh								+	+											?	+*			
C. glauca var. *alba*								+	+		?	?								–	+		+	+
C. govaniana Wall.								+	+											?	?			
C. lutea DC.	+		–				+	+	+		+	–							?	?	?		–	–
C. meifolia Wall.		+						+	+											–	–			
C. thyrsiflora Prain								?	?											–	–			
Dicentra formosa Walp.																					+[e]			
Fumaria indica Pugsl. (N. India)							+	+	–		+	+								–	–		+	+
F. indica Pugsl. (bazaar seeds)						+																		+[e]
F. micrantha Lag.								+	–			+								–	–			+*
F. officinalis L.							–	+	+			+							+	+	–			+[e]
F. vaillantii Loisel								+	+											+	–			
Berberidaceae																								
Berberis chitria D. Don																								
B. vernaculosa Hemsl. et E. H. Wils.																								
B. vulgaris L.																								

r, roots; *s*, stem; *l*, leaves; *f*, flower; *c*, capsule; *sd*, seeds; +, alkaloid present; –, alkaloid absent; ?, presence of alkaloid not definitely confirmed; blank space denotes part not available for investigation; +*, presence of alkaloid confirmed by two-dimensional paper chromatography; +[e], presence of alkaloid confirmed by paper electrophoresis; +[e*], presence of alkaloid confirmed both by paper electrophoresis and by two-dimensional paper chromatography. Approximate R_F values on Whatman No. 1 paper in butanol:glacial acetic acid:water (100 : 10 : 30): berberine, 0·59; coptisine, 0·44; chelerythrine, 0·54; sanguinarine, 0·48.

of the much wider distribution of this toxic alkaloid than has hitherto been suspected, the attendant risks of contamination of milk and other foodstuffs become more obvious. Many of the traditional uses of poppy-fumaria products in various parts of the world, particularly their inclusion in medicaments, are dangerous and should be carefully reviewed. It is obvious that, while sanguinarine was the first pure substance observed to produce glaucoma experimentally[10], many other substances can probably do so in varying degrees[10,11], and the possibility that endemic primary glaucoma results from chronic poisoning with some substance or another should be borne in mind. Such chronic poisoning could arise by the innocent ingestion of the responsible agent or could be the unrecognized side-effect of drugs used for legitimate therapeutic purposes. The present communication reviews the distribution of sanguinarine and related alkaloids in Nature, and points to the likelihood of their transmission to man in food and drugs, while milk as a possible vehicle is considered in the following article.

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EXPERIMENTAL TRANSMISSION OF SANGUINARINE IN MILK: DETECTION OF A METABOLIC PRODUCT

By Drs. SOHRAB A. E. HAKIM, VALERIE MIJOVIĆ and JAMES WALKER

National Institute for Medical Research, Mill Hill, London, N.W.7

DIETARY factors are known to affect the quality of milk, and taints and off-flavours are often caused by the ingestion by cows of a variety of weeds, perhaps the most familiar being the taint acquired by cream and butter made from the milk of cows that have eaten cruciferous plants. Milk, however, probably always contains, in trace amounts derived from the pasture or other feeding-stuffs, undesirable substances that do not declare their presence as frankly as those that produce taints. Our present concern is with the possibility that toxic poppy-fumaria alkaloids, and sanguinarine (I) in particular, may be transmitted to man in milk from cattle grazing on pastures containing poppy-fumaria weeds, as we have previously suggested[1], and we wish to report some model experiments in that connexion. A striking example of the transmission of toxic alkaloids in milk has recently been given by Schoental[2], who found that the administration of certain *Senecio* alkaloids to the lactating rat produced fatal liver lesions in the young without having any apparent effects on the mother or on her lactation, and she further made the suggestion that various liver disorders in childhood may be the result of poisoning by milk.

Evidence supporting the possibility of transmission of argemone alkaloids in milk was first obtained in India when argemone leaves were added to a goat's diet. Some toxic substance was obviously absorbed and transmitted, for feeding the goat's milk to four rhesus monkeys produced a rise in their eye-tension. A further experiment was made to determine if still higher levels of eye tension could be reached and maintained by reducing the cysteine content of the poisoned goat's milk. This was based on the human epidemiological records which showed that argemone poisoning was more severe in poorly fed communities and on our earlier animal experiments in which

cysteine had diminished or prevented the toxic effects of sanguinarine[1a]. Four monkeys were fed on a synthetic diet low in cysteine, prepared with the casein-fat portion of the toxic goat milk; in two animals the basic tension rose to much higher levels and decreased only slightly after about eight weeks. The results obtained with these monkeys confirmed the theoretical possibility that milk can transmit poisons that raise eye tension[1b]. Argemone leaves contain traces of sanguinarine together with other isoquinoline alkaloids (ref. 3 and preceding article), and it is possible that other alkaloids, also secreted in the goat's milk, contributed to produce the rise in eye tension observed in the above experiments. The goats, in spite of producing milk toxic to monkeys, showed only a slightly raised eye tension, and, as a species, goats are known to be resistant to certain other poisons[4].

In the experiments now to be described milk was examined by the following methods: (1) *Dialysis*. The milk was diluted, brought to the mean isoelectric point of its proteins, and dialysed through 'Cellophane'. The dialysate was concentrated under reduced pressure, acidified with acetic acid, and continuously extracted with chloroform for several hours. The aqueous phase was then made alkaline with sodium hydroxide solution, re-extracted continuously with chloroform, and finally with ether. The extracts were evaporated, and the combined residues were spotted on paper for chromatography or electrophoresis in the manner described in the preceding communication. (2) *Acid hydrolysis*. The milk was heated with an equal volume of 3 *N* hydrochloric acid at 100° C. for 4 hr., and the cooled mixture was then extracted continuously with organic solvents at both acid and alkaline *p*H as described in the preceding method. When sanguinarine was artificially added to control milk, the quantities afterwards recovered by dialysis were small, but acid hydrolysis led to greater recovery.

Lactating rabbits (2·5–3·0 kgm.) were separated from their young and injected subcutaneously in the flank with 4–8 mgm. of sanguinarine chloride in aqueous solution. At varying intervals during the next 4 hr., 5–10 units of oxytocin were injected, and the rabbits were milked by intermittent suction and massage. The milk was then processed as described above, and the extracts were examined by paper chromatography and paper electrophoresis. In four out of ten samples of rabbit milk obtained after injections of sanguinarine the alkaloid and a green-fluorescing metabolic product were detected by both methods. Several other weaker fluorescent spots, presumably representing other metabolic products, were also seen. All these were absent from control experiments with normal rabbit milk. The properties of the green-fluorescing metabolic product are discussed here.

With the assistance of Dr. D. R. Bangham, we succeeded in separating and detecting sanguinarine in as little as 1–2 ml. of the milk of rabbits injected with this alkaloid. The milk was electrophoretically differentiated on a column of 'ethanolysed' cellulose[5] in phosphate buffer, and collected serially in 50 fractions. Sanguinarine could only be detected after hydrolysis of the samples, and only in the albumin fractions. Many alkaloids are known to be strongly adsorbed on to serum albumin, and this was found to be the case for sanguinarine. After injecting sanguinarine into rats, cats and monkeys, 1 ml. samples of their plasma were collected and separated electrophoretically. As with the milk, sanguinarine was only found after acid hydrolysis and only in those fractions which contained serum albumin. Although present in most of their viscera, the maximum recovery of sanguinarine was from the liver.

In collaboration with Dr. A. H. Gordon we found that sanguinarine was converted in the liver into the green-fluorescing metabolic product. Sanguinarine chloride (1·8 mgm. in 5 ml. normal saline) was added to blood (50 ml.) which was mechanically circulated for 4 hr. through the isolated liver of a rat[6]. Blood samples were taken after 10, 30 and 60 min. and at the end of the experiment. All samples were hydrolysed with hydrochloric acid in the manner described above, and the hydrolysis mixtures were made alkaline with sodium hydroxide and extracted with chloroform. The residues from the chloroform extracts were taken up in about 0·5 ml. of chloroform–glacial acetic acid and spotted for electrophoresis on paper in 10 per cent formic acid. No sanguinarine was found at all, but the green-fluorescing substance was present in the 4-hr. specimen and there may have been a trace in the 60-min. specimen.

Properties of the Green-fluorescing Metabolic Product

This substance was best obtained from the urine of rabbits injected with sanguinarine chloride (1). Two rabbits were kept in metabolism cages and received injections of sanguinarine chloride (8 mgm.) daily for 5 days a week for 6 weeks and the urine was collected. The urine (2·5 l.) was acidified with concentrated hydrochloric acid (200 ml.) and heated on the water-bath for 2 hr. with the addition of an anti-foam. The cooled mixture was basified with sodium hydroxide solution and extracted with chloroform (about 1·5 l.). The emulsified organic phase was shaken with water until neutral and then stirred with anhydrous sodium sulphate until a clear chloroform solution was obtained. This process of extracting the hydrolysed urine was repeated four times. The residue obtained on evaporation of the combined chloroform extracts was applied to a column of alumina (activity I/II) (100 gm.), and eluted with benzene–acetic acid. The first fraction was shown by paper electrophoresis to contain the green-fluorescing material and several other fluorescent substances; none of these was observed on similar treatment of the urine from control rabbits receiving the same diet. The fraction containing the green-fluorescing substance was further purified by solution in benzene and extraction with 20 per cent hydrochloric acid. The acid solution was basified and extracted with chloroform. The chloroform solution was shown by paper electrophoresis to contain the green-fluorescing substance, and the material was chromatographed in dry benzene on alumina (10 gm.) as before. The first fraction, coming off the column as a blue-violet fluorescing solution, deposited a few minute colourless needles on evaporation and contained the substance sought as the sole fluorescent material (green on paper electrophoresis in acid solution); it was also present in the second fraction together with a substance showing a blue fluorescence on the acid paper electrophoresis strip, but none was present in subsequent fractions, which contained still more fluorescing substances (violet, blue) as shown by paper electrophoresis. The green fluorescing sub-

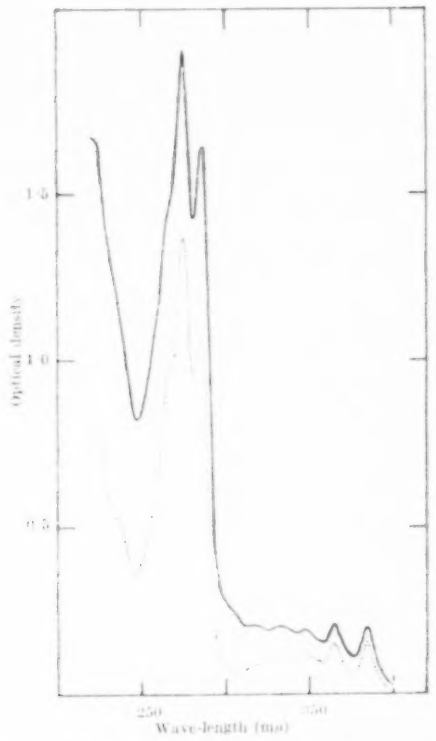
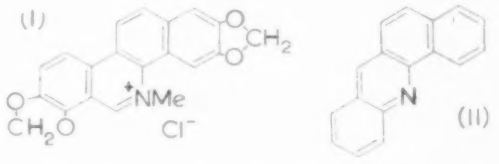


Fig. 1. Ultra-violet absorption spectra in spirit. ——— green-fluorescing metabolic product, extracted from paper electrophoresis strip (concentration unknown); ..... 3,4-benzacridine (0·42 mgm./100 ml.)

stance possessed numerous properties identifying it with a high degree of certainty with 3,4-benzacridine (II). A reference specimen of the latter substance was available *via* a hydrogenated derivative formed as a by-product in the preparation[7] of 3,4-benzophenanthridine, and it was later obtained by two unambiguous syntheses[8,9]. The ultra-violet absorption spectrum of the solution obtained by eluting the green-fluorescing metabolic product from the paper electrophoresis strip with ethanol showed a remarkable degree of correspondence with that of 3,4-benzacridine (II) (Fig. 1); and our colleague Dr. G. H. Beaven, who kindly examined the spectra of the two substances for fine structure by the logarithmic cam method[10] in ethanol both before and after the addition of 0·01 *N* hydrochloric acid, reported that the fine structure bands were identical in the spectra of the two substances. The metabolic product and 3,4-benzacridine showed identical behaviour on paper chromatograms and on paper electrophoresis strips, and the fluorescences of the two substances on paper were indistinguishable under acid (green) and alkaline (blue) conditions. Through the courtesy of Prof. R. T. Williams, St. Mary's Hospital Medical School, we were able to compare the fluorescence excitation and emission characteristics of the metabolic product eluted from paper electrophoresis strips with those of 3,4-benzacridine similarly treated using the Aminco-Bowman spectrophotofluorimeter. In 0·1 *N* hydrochloric acid both substances showed activation spectra with maxima at 305 and 390 mμ, exciting fluorescence with a single maximum at 495 mμ; when the solutions were made alkaline with sodium hydroxide a maximum in the activation spectra of both substances appeared at 300 mμ, exciting fluorescence with a maximum at 430 mμ. With a stronger (alkaline) solution of 3,4-benzacridine it was possible to observe another maximum in the activation spectrum at 390 mμ, but light-scattering prevented its observation with the weaker solutions obtained by eluting paper electrophoresis strips.

With so many criteria of identity satisfied, there can thus be little doubt that the metabolic product was indeed 3,4-benzacridine (II), and, if it arose from sanguinarine (and that conclusion seems inevitable), it must have resulted from a profound metabolic alteration for which we know of no close analogy. We have no precise measure of the extent of the conversion of one into the other, but it must be quite small. N-Demethylation calls for no comment, but, in addition, the oxygen functional groups have disappeared and a rearrangement of the carbon skeleton has taken place. Enzymic fission of alkyl aryl ethers[11,12] and metabolic dehydroxylation[11,13] are both well established metabolic reactions, so that the loss of the oxygen functional groups in the present instance may be regarded as extensions of these processes. The rearrangement of the carbon skeleton in passing from sanguinarine chloride (I) to 3,4-benzacridine (II) is possibly also not as bizarre as it would appear at first sight, as there are analogies *in vitro* in the dienone-phenol rearrangement[14], in the anthrasteroid rearrangement[15,16] and in the recently announced conversion of picene into 1,2 : 5,6-dibenzanthracene[17]. In each of these conversions one part of a condensed ring system exchanges its position of fusion with respect to the rest of the system for an adjacent position, and although only the last of these occurs in a fully aromatic system they presumably all proceed by way of transient spirocyclic intermediates and successions of 1,2-shifts[15,16,18]. A mechanism involving ring-chain tautomerism of an intermediate reduced derivative is, however, not excluded for the metabolic conversion of sanguinarine chloride.



It is obvious from these experiments that sanguinarine, together with some of its metabolic products, can be secreted in traces in rabbit milk, and application of the sensitive methods of detection developed in this and in the preceding communication to the milk of goats that have been fed on *Argemone* leaves has now shown the presence of small amounts of sanguinarine in such milk also. Considering the cosmopolitan distribution of poppy-fumaria weeds and the regularity with which sanguinarine occurs in these plants, the likelihood of traces of sanguinarine and of other toxic alkaloids finding their way into milk supplies intended for human consumption must be quite considerable. Under field conditions and in good pastures the unpleasant odour and taste of

various *Papaver* spp. render these plants objectionable to animals[19], which frequently show considerable discrimination in their eating habits, but it is otherwise with hay and silage. On the other hand, the common fumitory (*Fumaria officinalis* L.), which is widely distributed and fairly common, is readily eaten by cows though not by goats[20]. Under adverse conditions and in poor neglected pastures cattle are obliged to feed more indiscriminately and the likelihood of alkaloidal contamination of milk in such circumstances must be considerably greater. Whether or not these observations have a bearing on the incidence of endemic primary glaucoma cannot at present be assessed, and they are merely offered as circumstantial evidence to show that regular unintentional absorption of minute amounts of sanguinarine and of other papaveraceous alkaloids by man is feasible.

We wish to thank Dr. D. R. Bangham, Dr. G. H. Beaven, Dr. A. H. Gordon and Prof. R. T. Williams for their generous assistance. One of the authors (S.A.E.H.) is grateful to Sir Charles Harington for hospitality at the National Institute for Medical Research, to the Wellcome Trust for financial support, and to Lady Mellanby and the late Sir Edward Mellanby for their help and encouragement.

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MAMMARY CANCER INDUCED BY A SINGLE FEEDING OF POLYNUCLEAR HYDROCARBONS, AND ITS SUPPRESSION

By Prof. CHARLES HUGGINS, LORRAINE C. GRAND and FILOMENA P. BRILLANTES
Ben May Laboratory for Cancer Research, University of Chicago

ONE of the most remarkable experiments in cancer research is the induction of cancer which occurs preferentially in the breast of rats following the feeding of carcinogenic hydrocarbons. The first compound found to incite mammary cancer by this method was 2-acetylaminofluorene (2-AAF) which was incorporated in a diet that was fed to rats for many months[1]. The repeated daily administration of 3-methylcholanthrene (3-MC) to young adult female rats of a special strain induced mammary cancer invariably and rapidly[2,3]; the earliest cancer of the breast was detected by palpation 20 days after beginning the feeding, and within two months every animal had developed multiple tumours of this sort. A newly recognized property[2] of the mammary cancers induced by this method was the dependence of many of the tumours on the presence of hormones, since regression takes place after ovariectomy or certain other endocrine procedures. This is a characteristic that is commonly observed in cancer of the breast in human beings, but which is unique among mammary cancers available in the laboratory.

It will now be shown that a single feeding of polynuclear hydrocarbons to rats caused selective injuries in the recipient rather than total body damage. These lesions include the induction of leukopenia and of cancers of two types, carcinoma of the breast and of the external acoustic duct. Further, established mammary cancers were suppressed in many rats by treatment with certain hormones or by pregnancy.

The induction of mammary cancer following the application of aromatic carcinogens remotely from the breast was first observed by Maisin and Coolen[4] who painted the skin of mice with 3-MC and observed a high incidence of cancer of the breast in addition to cancer of the skin. A single intramuscular injection of carcinogenic hydrocarbons is a classical method of evoking sarcoma in susceptible rodents[5]. An injection of 3-MC into the breast of mice gave rise to sarcoma and adeno- and squamous carcinoma of the mammary glands[6]. A single intravenous dose of urethane gave rise to benign pulmonary tumours in mice[7].

Induction of Mammary Cancer

Female rats of the Sprague Dawley strain were used in all the experiments, with 10 rats in each experimental group: unless stated otherwise, the animals were age 50 days and weighed 140–150 gm. when the hydrocarbons were fed. They remained free from respiratory diseases.

With the aid of gentle heating, 2 gm. of 7,12-dimethylbenz(a)anthracene (DMBA), or 1·5 gm. of 3-MC was dissolved in 100 ml. of sesame oil. One gram of 2-AAF was dissolved in 10 ml. of ethanol and the solution was diluted to 100 ml. with sesame oil. The solutions were instilled in the stomach through a soft rubber catheter, and only a single dose was administered. The rats were examined frequently for palpable tumours for 150 days and cancers weighing 10 mgm. or more were readily detected. The occurrence of the cancers was dated from the day of feeding the carcinogen. The tumours were confirmed

at necropsy when the total number of visible tumours ('active centres') was counted.

In our rat colony two 'spontaneous' mammary cancers have been observed among about 20,000 untreated female rats less than eight months of age. But benign mammary tumours occur very frequently in this strain in senescence[5].

3-*Methylcholanthrene*. A single feeding of 3-MC (100 mgm.) induced cancer in 100 female rats, aged 50–65 days, in 10 consecutive series; no tumours were observed in 20 males treated similarly. The rats suffered a decline in body-weight (total loss 10–15 gm.) for 48 hr. after the feeding, but a gain in weight was observed on day 3. In these series o females, mammary cancer was developed in every rat and squamous carcinoma of sebaceous glands adjacent to the external auditory canal in two of them; no other tumours were found. The earliest mammary cancer was detected by palpation on day 31, and the last was observed on day 130. But in serial histological sections of the inguinal mammary glands o 10 rats, 14 days after a single feeding of 3-MC, carcinomata were found in two of the glands on microscopic examination. The squamous carcinomata of sebaceous glands appeared, respectively, on days 109 and 121.

The influences of age at the time of a solitary feeding, and of the presence of the ovaries, were investigated by feeding a single dose of 3-MC (66·6 mgm./100 gm.) to rats of various ages; half the animals were intact, and the ovaries of the others had been removed at the time of weaning. In the intact rats mammary cancer was induced by feeding the carcinogen at age 23 days and the incidence o tumours rose progressively with age until all rats fed 3-MC at age 50 days developed cancer of the breast (Table 1). There was a decline in the incidence of mammary cancer in rats fed 3-MC at age 75 days, and cancer of the breast developed in only a small number of animals fed 3-MC at age 100–365 days (Fig. 1).

No mammary cancer was observed in 100 rats that had been ovariectomized at age 22 days and fed a single dose of 3-MC thereafter at various ages between 23 and 100 days.

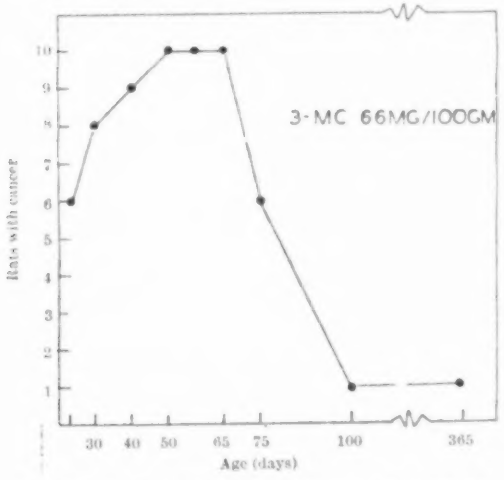

Fig. 1. Incidence of mammary cancer in groups of ten rats fed 3-MC once only. The abscissa indicates the age when the compound was fed

Table 1. Induction of Mammary Cancer by Intragastric Installation of Polynuclear Hydrocarbons at 50 Days of Age

Compound	Dose (mgm.)	No. with cancer*	Appearance of palpable tumours (days)			Active centres
			range	median	mean	
DMBA	20	10	28–50	41	42·8 ± 10·†	6·8
DMBA	15	10	34–70	49	48·5 ± 11	3·0
3-MC	100	10	31–86	50	51·3 ± 16	2·3
3-MC	50	8	35–121	56	61·4 ± 30	1·1
3-MC	25	7	34–54	49	47·5 ± 9	2·4
3-MC	10	5	45–129	52	75	1·3
3-MC	5	2	50 and 133	—	—	1·0
3-MC	2	1	48	—	—	1·0
2-AAF	100	3	43–73	53	56·3	1·0
2-AAF	50	3	51–79	59	63	1·0

* There were ten rats in each group. The animals were observed for 150 days.
† Standard deviation.

The optimal dose of 3-MC for the induction of mammary cancer after a single feeding was 100 mgm.; this dose induced 1–4 active centres in each rat. A single dose of 3-MC (2 mgm.) induced mammary cancer in one rat and there was a progressive increase in the rate of tumour incidence and in the number of active centres with augmentation of the dose until the optimal amount was reached (Table 1).

A large portion of 3-MC which is fed passes through the alimentary tract. After a large dose the faeces were highly fluorescent. Our colleagues, Dr. Flesher and Dr. Sydnor, fed a single dose of tritium-labelled 3-MC (10 mgm.) to rats and recovered about 90 per cent of the administered radioactivity in the faeces, where significant quantities were detected for 7–11 days following the single feeding[6].

Trace amounts of 3-MC are sufficient to induce mammary cancer. Compressed, cylindrical pellets of known weight were implanted in the spleen of 18 rats; neoplasms did not arise in the spleen but three of the animals developed mammary cancer at 105, 148 and 199 days respectively. At necropsy, the pellets were removed from the spleen, blotted, heated to 100° for 24 hr. and re-weighed. No decrease in weight of the 3-MC pellet occurred during the long sojourn in the spleen. In one of the experiments wherein a rat developed mammary cancer at 148 days after implantation of 3-MC in the spleen, both the original and final weight of the pellet was 26·8 mgm. An amount of 3-MC too small to be detected on our balance had induced mammary cancer. Shear[7] observed formation of sarcoma in muscle after implanting therein a pellet of cholesterol containing dibenz(a,h)anthracene (0·4 µgm.).

7,12-*Dimethylbenz(a)anthracene*. A single feeding of DMBA was highly effective in the induction of mammary cancer in female rats. DMBA (1 mgm.) induced mammary cancer, and there was a progressive rise in the incidence of cancers with increased dosage until the optimal dose was reached (Fig. 2). The optimal dose of DMBA (dissolved in sesame oil, 1 ml.) for induction of mammary cancer by a single feeding was 20 mgm. For: (1) every rat survived; (2) mammary cancer developed in 40 consecutive rats without exception; (3) the first cancer was detected by external examination at 28 days and all the rats had visible tumours of the breast before 60 days; (4) the number of active centres in individual rats varied from 3 to 21, the average being 6·8. DMBA (15 mgm.) induced mammary cancer in every rat after a single feeding, but there were fewer active centres than in rats which had received 20 mgm. (Table 1). All 10 rats which were fed DMBA (50 mgm.) died 2–28 days afterwards.

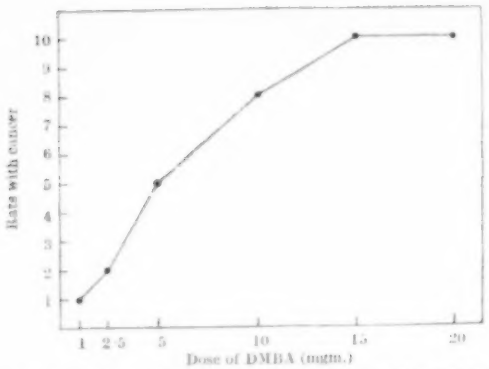

Fig. 2. Incidence of mammary cancer in groups of ten rats fed DMBA once only

It is known that the application of large amounts of 3-MC to the skin of mice causes leukopenia[10]. The leukocytes of the blood of rats were counted in quadruplicate before and at frequent intervals following a single feeding of DMBA (20 mgm.) to rats 50 days old. There was no change in their number for 24 hr., but leukopenia developed shortly thereafter and it was long-lasting (Fig. 3). The steady increase in body-weight of the young rats was interrupted for two days but growth recommenced thereafter (Fig. 3). But the sexual rhythm, demonstrated in the regular recurrence of œstrus cycles, was not delayed by feeding the carcinogen: œstrus appeared every 4–15 days both in DMBA-fed and in untreated control rats. It is clear that DMBA induced cancers and leukopenia and also caused a temporary cessation of body-growth, but brought about no significant decrease in the production of gonadotrophin by the hypophysis or in function of the ovary.

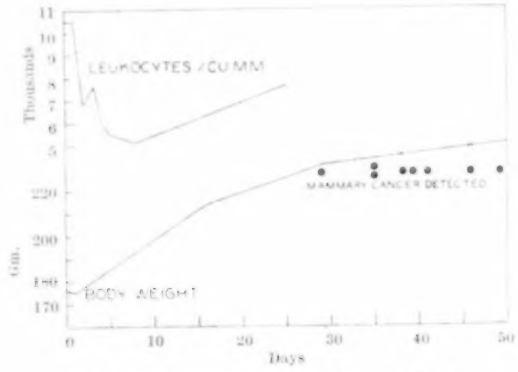

Fig. 3. DMBA (20 mgm.) was fed at day 0 to eight rats

2-Acetylaminofluorene. Feeding single doses of 2-AAF was a relatively inefficient method of inducing mammary cancer (Table 1). Twenty rats (50 days old) were fed an alcohol-containing solution of 2-AAF (50 or 100 mgm.) and six of them developed cancer of the breast within five months; no other tumours were observed. The chief interest of this compound was in its anæsthetic effects which were apparent after doses of 75–100 mgm. Due to its limited solubility in oil, 2-AAF was usually given in two divided doses separated by a 4-hr. interval. The rats became drowsy within 1 hr. after the first dose and were asleep within 2 hr. after the second feeding. They remained unconscious and did not move their position in the cage for 24 hr., but most of them woke within a few hours thereafter. Control rats fed sesame oil containing 10 per cent ethanol were not anæsthetized. Moreover, anæsthesia was induced in rats by feeding a dose of 75 mgm. of a solution of 2-AAF which contained no ethanol; for reasons of solubility the solution was administered at a temperature of 43°. Likewise, profound anæsthesia was induced by a single feeding of 2-aminofluorene (150 mgm.) dissolved in sesame oil, 3 ml., containing no ethanol.

Suppression of Mammary Cancer

At 50 days of age, normal female rats were fed a single dose of 3-MC (100 mgm.) and divided into groups. This feeding was the only experimental variable in the control rats which were maintained as virgins, and all developed mammary cancer (Table 2). Indeed, we have shown above that a single feeding of 3-MC (100 mgm.) induced mammary cancer without exception in normal female rats of this age, and that the tumours were demonstrated although not visible to the unaided eye after two weeks. Accordingly, at 65 days of age, the endocrine status of rats in many of the groups was modified drastically by breeding or by administration of steroid hormones.

The expected incidence of mammary cancer was lessened notably in rats bred 15 days after their solitary feeding (Table 2). Moreover, the daily injection of progesterone (4 mgm.) or of œstradiol-17β (10 μgm.) beginning at age 65 days, caused a similar decrease in the rate of incidence. The combined administration of progesterone (4 mgm.) with œstradiol-17β (1 or 10 μgm.) each day for 50 days induced the characteristic gestational type of hyperplasia of the mammary glands, which resembles that found in rats on day 15 of pregnancy, but few mammary cancers ever developed in these rats (Table 2); the neoplasms had been suppressed by the hormonal treatments.

In earlier work[11] the repeated feeding of 3-MC to rats at the onset of pregnancy, or to other animals

Table 2. SUPPRESSION OF MAMMARY CANCER IN PREGNANCY AND IN RATS INJECTED DAILY FOR 50 DAYS BEGINNING 15 DAYS AFTER A SINGLE INTRAGASTRIC INSTILLATION OF 3-MC (100 MGM.)

Steroids injected	No. with cancer	Appearance of palpable tumours (days)			Active centres
		range	median	mean	
None: normal female	10	46–84	56	58·3 ± 11	1·6
None: pregnant	6	30–76	50	48·6 ± 18	2·2
Progesterone (4 mgm.)	8	35–121	46	61·4 ± 30	2·0
Œstradiol-17β (10 μgm.)	7	77–115	97	96·3 ± 13	2·3
Progesterone (4 mgm.) and œstradiol-17β (10 μgm.)	2	42 and 121	—	—	1·0
Progesterone (4 mgm.) and œstradiol-17β (1 μgm.)	3	42–133	45	—	1·0
Progesterone (4 mgm.) and œstradiol-17β (0·01 μgm.)	8	36–120	43	51·9 ± 28	3·2

There were 10 rats in each group and 3-MC (100 mgm.) was administered to every rat at age 50 days. All the animals were virgin females except one group which were bred between age 65 and 68 days; steroids were not administered to these groups. In the others, hormones dissolved in sesame oil (0·2 ml.), were injected intramuscularly 6 days each week for 50 days beginning at 65 days of age. The rats were observed for 150 days.

injected with large quantities of equine gonadotrophin[3], seldom induced mammary cancer. The present experiments demonstrate an effect of a different kind since they show that oestradiol with progesterone, while inciting brisk growth of normal mammary glands, often destroyed the young cancers induced within the previous two weeks by a large dose of 3-MC.

Discussion

Induction of cancer by a solitary feeding of polynuclear carcinogens emphasizes the high importance of the alimentary tract as a portal for their entry and, indeed, of a single meal for the development of mammary cancer in the rat. This method has advantages over multiple feeding in its extreme simplicity and in saving of labour and of rare or costly compounds associated with equal rapidity, and invariability of development of multiple mammary cancers. A stoichiometric relationship exists between the dose of effective carcinogens and the rate of incidence of the tumours, together with their number. The mammary cancers arise under highly restricted conditions, but these are easily fulfilled. All young adult female rats of the Sprague–Dawley strain fed an optimal amount of DMBA developed mammary cancer under the favourable hormonal conditions which prevail in them. Pregnancy, or the administration of progesterone with oestradiol, frequently destroyed many young cancers that were obtaining a foothold, and rats in this class never suffered a recrudescence of their mammary cancers.

Not all the cells of the body were injured by a single moderately large feeding of DMBA and lesions developed selectively. The haematopoietic and lymphatic systems were damaged and two types of cancer were induced, while the production of gonadotrophin by the hypophysis, and of phenolic oestrogens by the ovary, were undisturbed.

Not all the cells of the responding animals became malignant after feeding the effective polynuclear hydrocarbons; cancer developed only in the mamma and in special sebaceous glands, while sarcoma was never encountered. All the mammary cancers were adenocarcinomata and squamous carcinoma was not observed in the breast. Yet in companion rats the intramuscular injection of the effective carcinogens evoked sarcoma, locally, in most of them when these carcinogens were injected in muscle. The properties which endow special cells of the body with selective vulnerability to trace amounts of polynuclear hydrocarbons are unknown.

Not all the many millions of cells of the mammary glands became malignant after feeding effective amounts of the carcinogens. The maximal number of mammary cancers which has been observed in this laboratory after a single feeding is 21. A threshold response to the hyperconjugated hydrocarbons is involved in certain cells of the mammary gland in the induction of cancer of the breast by hydrocarbons, since a minimal effective dose gives rise to only one active centre.

Berenblum[12] has postulated that carcinogenesis develops in multiple independent stages. The present experiments demonstrate that mammary cancer, under the stated conditions, arises in a single step.

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TERMINOLOGY IN PLANT- AND SOIL-WATER RELATIONS

A RECENT article[1] under the above title seems unnecessarily complicated and in some respects misleading.

Consider the transfer of water, through a membrane permeable only to water, from a solution α at temperature T, at pressure P^α, and having concentration(s) m^α of solute(s), to a solution β at temperature T, at pressure P^β, and having concentration(s) m^β of solute(s). Water will pass spontaneously from solution α to solution β, *or* the two solutions are in equilibrium, *or* water will pass spontaneously from solution β to solution α, according as:

$$\mu_w(T,P^\alpha,m^\alpha) - \mu_w(T,P^\beta,m^\beta) \gtrless 0 \qquad (1)$$

where $\mu_w(T,P,m)$ is the chemical potential of water in a solution at temperature T, at pressure P, and having concentration(s) m of solute(s). We now identify β with pure water at temperature T and at atmospheric pressure by putting $P^\beta = 1$ atm. and $m^\beta = 0$, and define a dimensionless number W called the 'water number' of the solution α (whether α is a solution in a beaker, a compressed solution in a turgid cell, soil-water surrounding the roots of a plant, or otherwise) by the relation:

$$W = \{\mu_w(T,P^\alpha,m^\alpha) - \mu_w(T,1\text{ atm.},0)\}/RT \qquad (2)$$

where R is the gas constant. The water number W is then an exact thermodynamic discriminant determining according to its sign whether pure water will flow into (< 0), or out of (> 0), the solution α. Similarly water will flow from a solution with water number W_2 to a solution with water number W_1 if $W_2 > W_1$ and conversely. A solution with a negative water number 'wants' to gain water; a solution with a positive water number 'wants' to lose water.

In order to express the water number in terms of more familiar experimental quantities we begin by rewriting equation (2) in the form:

$$RTW = \{\mu_w(T,P^\alpha,m^\alpha) - \mu_w(T,1\text{ atm.},m^\alpha)\} + \{\mu_w(T,1\text{ atm.},m^\alpha) - \mu_w(T,1\text{ atm.},0)\} \qquad (3)$$

and then evaluate the two terms separately. With only trivial inaccuracy we then obtain the following set of thermodynamically equivalent relations; which one is used, is entirely a matter of experimental convenience:

$$W = (P^a - 1 \text{ atm.})V_w/RT + \ln (p_w/p^\circ_w) \qquad (3a)$$

where V_w is the molar volume of water, p_w is the partial pressure of water over the solution, and p°_w is the vapour pressure of pure water:

$$W = (P^a - 1 \text{ atm.})V_w/RT - k_f \Delta T_f \qquad (3b)$$

where k_f is the cryoscopic constant of water and ΔT_f the lowering of the freezing point (equation 3*b* is, of course, restricted to 0° C.):

$$W = (P^a - 1 \text{ atm.})V_w/RT - k_b \Delta T_b \qquad (3c)$$

where k_b is the ebullioscopic constant of water and ΔT_b the elevation of the boiling point (equation 3*c* is, of course, restricted to 100° C.), and:

$$W = (P^a - 1 \text{ atm.})V_w/RT - \Pi V_w/RT \qquad (3d)$$

where Π is the osmotic pressure of the solution.

Of the four methods of measuring the second term in equations (3) the third has in practice been used scarcely at all, while the first and second have been used much more often, and usually with much higher accuracy, than the fourth. Results obtained by any of these four methods are often expressed as osmotic coefficients φ in terms of which we have the alternative relation:

$$W = (P^a - 1 \text{ atm.})V_w/RT - M_w \varphi m^a \qquad (3e)$$

where M_w is the molar mass of water and m^a is the sum of the molalities of all the solutes in the solution. Tables of φ for solutions of common solutes (including sucrose) are available[2].

Equations (3*a*) to (3*e*) are thermodynamically equivalent. Equation (3*d*) can be rearranged in terms of quantities with the dimensions of pressure as follows:

$$-RTW/V_w = \Pi - (P^a - 1 \text{ atm.})$$

or in terms of a few of the names commonly used by botanists: suction pressure (or diffusion pressure deficit) = osmotic pressure − wall pressure (or turgor pressure). In my opinion the apparent simplicity of this formulation, together with the traditional preoccupation of botanists with osmotic pressures to the neglect of more important ways of measuring essentially the same quantity, has led to a great deal of confusion, misunderstanding and pointless argument (as well as to the corruption of mechanical terms such as 'pressure', 'force', 'stress' and 'potential'). In particular, while the wall pressure is the actual excess pressure over 1 atm. in a more or less turgid cell, neither the suction pressure nor the osmotic pressure is an actual pressure in any part of a plant during its approach to equilibrium with its surroundings.

The definition of water number can easily be extended to systems where variables other than pressure and concentration are important. For example, if the difference of heights $h^\alpha - h^\beta$ is important (as in a tall tree) the gravitational term $M_w g(h^\alpha - h^\beta)$ must be added to the left-hand side of equation (1).

Water numbers and indeed any thermodynamic treatment can, however, only be applied to a given system (for example, soil + plant + air) when the whole of that system is at one and the same temperature (cf. par. 6 of ref. 1, where the contrary is stated).

The application of water numbers to practical botany will be described more fully elsewhere.

M. L. McGlashan

Department of Chemistry,
The University,
Reading.

[1] Slatyer, R. O., and Taylor, S. A., *Nature*, **187**, 922 (1960).
[2] Robinson, R. A., and Stokes, R. H., "Electrolyte Solutions", 461 (Butterworths, London, 1955).

Dr. McGlashan's concept of 'water numbers' is an alternative step in the direction suggested by the delegates to the Unesco–Spain symposium on plant water relations in arid regions[1]. It, too, proposes a single term to replace the larger number at present in use and has simply and clearly partitioned this quantity into measurable components.

However, as a substitute for the proposals it does not encompass the identifiable components that may contribute to the 'water potential'. The symposium delegates felt that the additional factors which were recognizable should be given consistent names, whereas the use of 'water numbers' provides a name for the total potential only.

In general terms, the symposium delegates were keen to develop a terminology which would be more comprehensive than the existing plant water systems. To this extent, pressure, matrix and osmotic components were introduced, recognizing that, for example, the matrix term might not be necessary to evaluate the total water potential in plants or the osmotic component necessary to evaluate the total components in soils. It was also envisaged that other component potentials due to external force fields, such as gravity and electricity, could be included if necessary or desirable.

Dr. McGlashan's proposal of 'water numbers' is identical with our 'water potential' (that is, the difference in the Gibbs function for the single component, water, in a multiple component system and the same component in the reference state). He does not provide for naming the several factors that contribute to the overall water potential as we have done. His equations 3*a*–3*e* are equivalent relations expressed in terms of various methods that might be used to evaluate the chemical potential under standard laboratory conditions. These equations all represent standard methods for evaluating the chemical potential of water in pure systems.

Methods based on evaluation of the freezing or boiling point of water are subject to errors of unknown magnitude since they assume that the entropy and enthalpy of the water in system behave the same as those of pure free water. This is known to be incorrect at least for soil water[2], so that the values determined by these methods can be applied, without error, only at the freezing and boiling temperatures.

The application of the classical Gibbs function (and hence the water number) to systems that are not at constant temperature is not possible because flow of heat occurs whenever there are temperature differences. This upsets the equilibrium conditions, thus invalidating the equilibrium thermodynamics. This is also true in any system in which any kind of flow is taking place. It is still possible, however, to use thermodynamic concepts and terminology for non-equilibrium systems, if the change in entropy of the system is considered[3]. The terminology proposed by the delegates to the Unesco–Spain symposium is

adaptable to applications of thermodynamics to irreversible processes, hence temperature differences may be included in the terminology. Likewise, the water potential (or water number) determined on a system in equilibrium at one temperature will be different from the water potential of the entire system in equilibrium at another temperature, therefore it is necessary to consider a temperature (and hence an entropy) contribution to the water potential.

It might be mentioned that at the request of the symposium delegates, we also circulated the proposals to a large number of scientists known to be interested in the subject of terminology in plant–soil–water systems. The range of response varied from complete rejection to complete acceptance, with most correspondents being in favour of general acceptance with some modifications. In general, most scientists concerned with either soil– or plant–water relations alone considered that either the existing terminologies were satisfactory, or that the new proposals compromised the existing ones to a degree that was not of benefit. The majority of scientists concerned with the interacting plant–soil–water system were, on the other hand, keen to have a more unified form of expression. These varied opinions have been summarized, and the original proposals modified to include as many of the comments as possible. The resultant document will be published shortly by Unesco, in the Proceedings of the Madrid symposium.

The original proposals were also discussed at the recent congress of the International Soil Science Society at Madison, Wisconsin. Here again a wide range of response was encountered, and Commission I (Soil Physics) of the International Society of Soil Science has appointed a committee to investigate the subject of soil water terminology.

R. O. Slatyer
Division of Land Research and Regional Survey,
Commonwealth Scientific and Industrial
Research Organization, Canberra.

S. A. Taylor
Department of Agronomy,
Utah State University, Logan, Utah.

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RADIAL PARTICLE DISPLACEMENTS IN POISEUILLE FLOW OF SUSPENSIONS

By Dr. G. Segré
Cartiera Vita Mayer and Co., Milan
AND
Dr. A. Silberberg
Weizmann Institute of Science, Rehovot, Israel

We have observed that macroscopic spherical particles collect into a thin, annular region when an initially uniform dilute suspension is passed in laminar flow through a straight tube. The development of the effect is proportional to the length l of the tube, to the mean velocity V of flow and to the fourth power of the ratio of particle radius a to tube radius R.

Our equipment consisted of the flow apparatus, an optical scanning device and an electronic counting circuit. Spheres of polymethyl methacrylate, in various uniform fractions of diameters between 0·8 and 1·6 mm., were suspended in a liquid of the same density $\rho = 1{\cdot}18$ gm./c.c. and of high viscosity $\eta = 400$ cp.). The flow apparatus consisted of a vertical tube of variable length, diameter 11·6 mm., terminating in two containers with the necessary stirrers and pressure-head regulators. At a selected cross-section of the tube, two narrow mutally perpendicular light rays could be made to traverse it without distortion and thus to determine a precisely selected small region at their crossing. Two photocells and a coincidence circuit permitted the computation of the actual number of particles which passed the point of intersection. From this number the average concentration of the suspension, as a function of the distance from the axis of the tube, could be calculated by dividing by the local velocity of flow.

The results are symmetrical about the axis, and are independent of the shape of the mouth of the tube. At very low velocities of flow, or at small distances from the input end, the particle count follows a parabolic distribution, showing that the concentration is constant over the entire cross-section (curve 1, Fig. 1).

At cross-sections farther down the tube, distributions of the type shown in curves 2 and 3, Fig. 1, are observed. In terms of particle concentrations (assuming the same parabolic velocity distribution as at the mouth) the results conform to the 'tubular pinch' effect illustrated in Fig. 2.

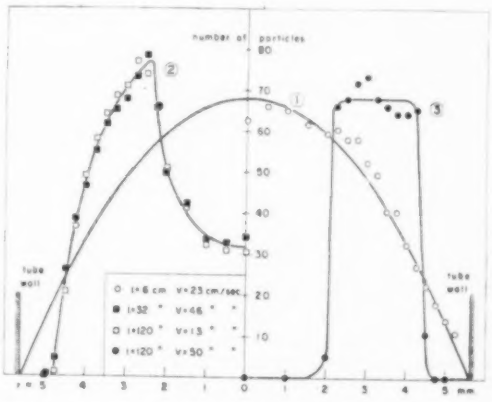

Fig. 1. Number of particle passages as a function of radial position in tube for a given total throughput (uncorrected for finite scanning cross-section). Particle radius 0·8 mm., initial concentration 1 part./cm.[3]

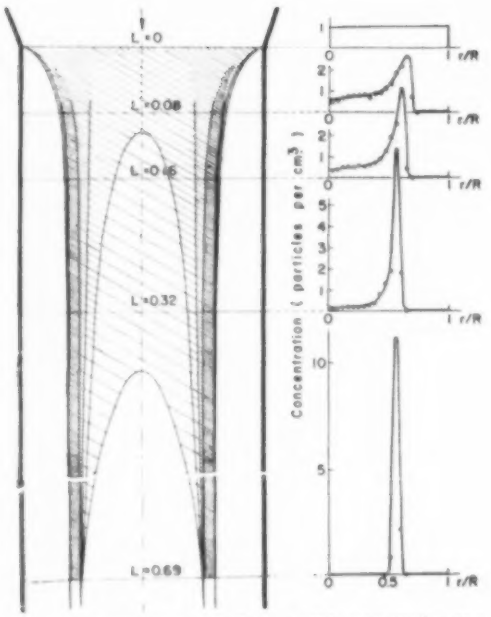

Fig. 2. The 'tubular pinch' effect: particle concentration as a function of radial and longitudinal position in tube. Initial concentration 1 part./cm.³. Concentrations are indicated by shading: closest shading (more than 2 part./cm.³); next (1–2 part./cm.³); next (0·5–1 part./cm.³); lightest shading (0–0·5 part./cm.³)

The results in Fig. 2 are plotted in terms of a reduced tube radius (r/R) and tube length:

$$L = (a/R)(av\rho/\tau_t)(l/R)$$

where $v = (a/R)^2 V$, and $(av\rho/\tau_t)$ can be defined as a relative particle Reynolds number[1]. All our results can be superimposed when plotted in these coordinates, that is, the same particle distributions are reached at corresponding positions L in the tube. The dependence of L on the relative particle Reynolds number, or more explicitly on the product Vl, can be shown to imply a radial particle velocity proportional to V^2. The force responsible for the effect thus originates in the inertia of the fluid.

Particle re-arrangements in parabolic flow have been suspected in the past, and certain anomalous flow-behaviour of suspensions has been explained in this way. Causes other than inertia forces have, however, been made primarily responsible as no direct observations of particle movements were made. Deviations from the Einstein viscosity equation (sigma effect) were explained by wall effects[2] and the criterion of minimum energy dissipation[3].

Some direct observations of particles concentrating in the central region of the tube[4] have been reported, but the relevant experiments seem to be of low precision or may have been complicated by electrostatic and other phenomena, as, for example, in the case[5] often quoted of red cells moving into the axis of blood capillaries.

On the theoretical side, the effects of fluid inertia have almost always been neglected in view of the difficulty of solving the complete Navier-Stokes equations of motion. Cases such as ours are thus explicitly excluded from available analyses of tube flow. The only way in which quadratic terms have been allowed for in a few cases[6,7] is through the inclusion by postulation of a transverse force which, as in the 'Magnus effect', arises from the combination of a rotatory and a translatory motion relative to the undisturbed flow of the fluid. It can be shown[8] by solving the linearized equations of motion that a spherical particle carried along by an unbounded parabolic field of flow is subjected to a couple and to a longitudinal force which give rise to a rotation and a translation, each proportional to the mean velocity of flow. Adopting the formalism of the Magnus effect, one can substitute these velocities in the Kutta-Jukowsky formula and obtain a force:

$$f = -k(a^3 V^2 r\rho/R^4)$$

and a radial velocity $\dot{r}$ corresponding to this force:

$$\dot{r} = -(k/6\pi)(a/R)^4(V^2\rho r/\tau_t)$$

proportional to V^2, as observed, but directed inwards only. In our case the radial force acting on the spheres is centripetal at the wall but centrifugal at the centre. A stationary distribution is thus reached, and the value of (r/R) where the particles concentrate seems to be independent of all other variables.

It is worth noting that if we assume for the dimensionless coefficient k the value suggested by Tollert[7] or that calculated by Saffman[8], agreement in order of magnitude with the observed centripetal removal of a particle from the wall is obtained.

This approach does not explain the strange dependence of the force on the distance from the centre with its reversal of sign. The curvature of the field of flow is patently insufficient to account for this behaviour. It is in the presence of a rigid wall at $r = R$ that the explanation must be sought. It should be noted that symmetry requirements are satisfied, as a force proportional to r, and thus, vanishing at the centre, is consistent with the observed removal of particles in the vicinity of the tube axis. On the other hand, the criterion of minimum energy dissipation according to which one would expect the particles to congregate in the centre is contravened.

The results exemplified by Fig. 1 are independent of the overall particle concentration up to the largest volume fraction (0·4 per cent) used by us, and a linear superposition of the effect is observed when particles of two different sizes are examined simultaneously. The points represent averages involving at least 20 separate experiments and the scatter shown in the diagrams is representative of the precision obtained.

The effect may be important in explaining certain anomalous flow behaviour of suspensions and may find application in the fractionation of particles of different size.

To the best of our knowledge the centrifugal effect has not previously been observed nor are any theoretical predictions extant. The investigation is being pursued, and a full report will be published elsewhere.

Acknowledgements are due to Prof. A. Katchalsky for many valuable discussions and to Cartiera Vita Mayer and Co., Milan, for enabling one of us (G. Segré) to carry out this investigation at the Weizmann Institute.

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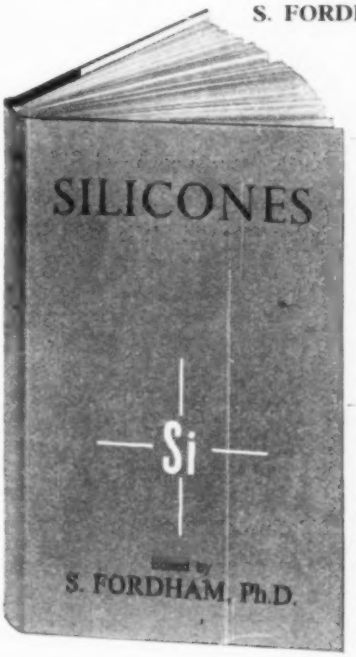

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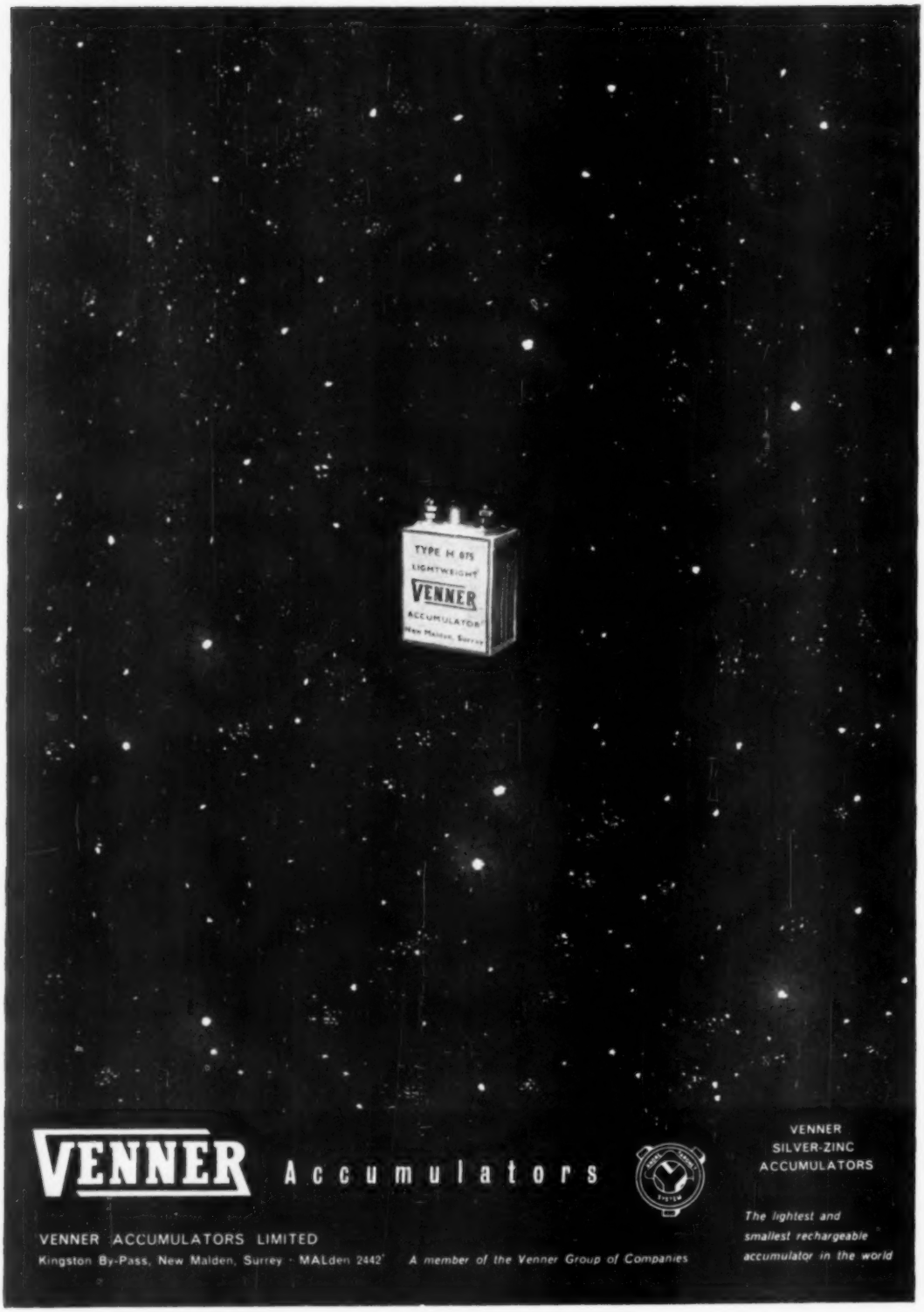
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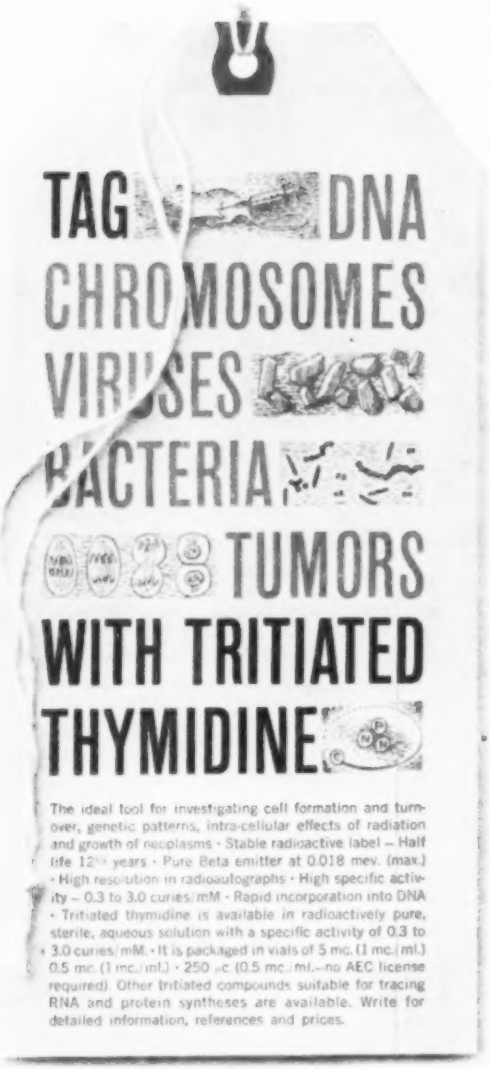
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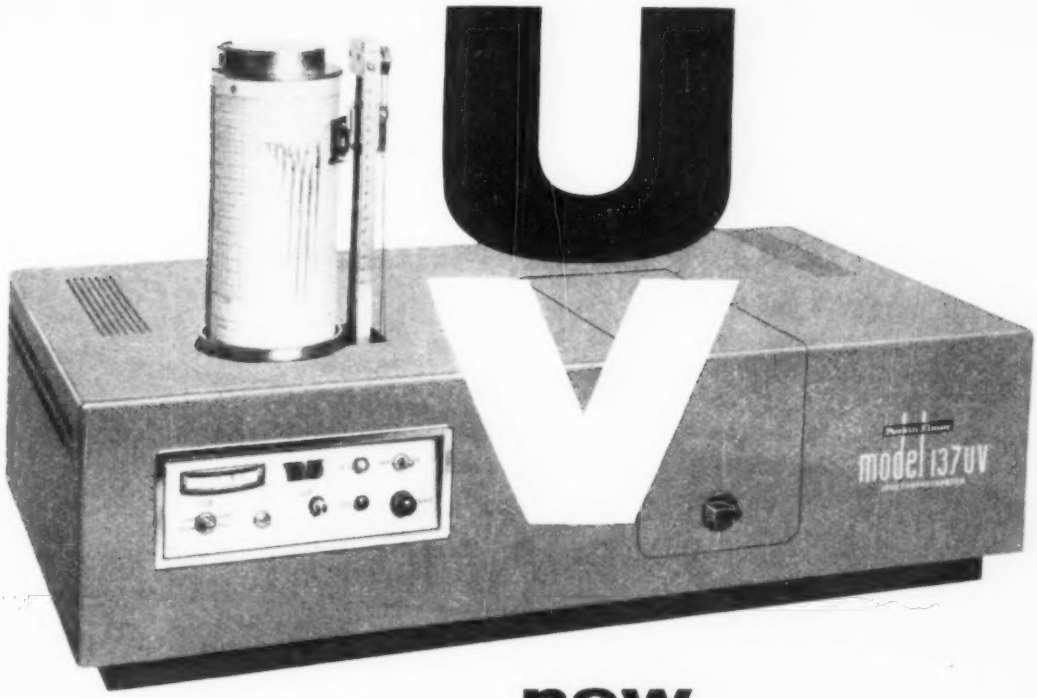

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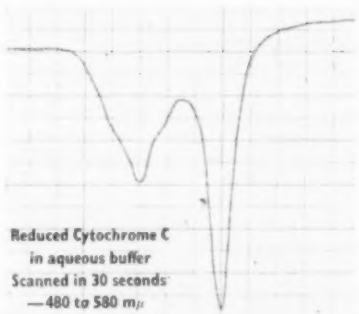

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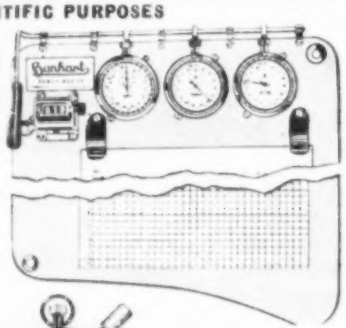

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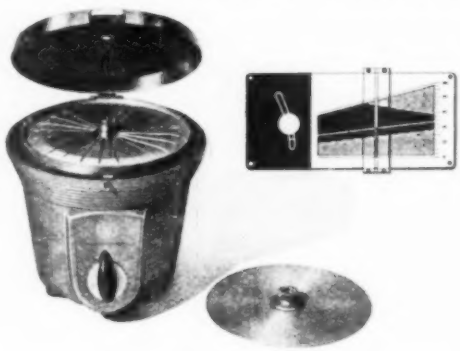

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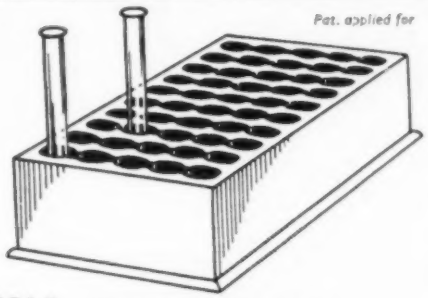

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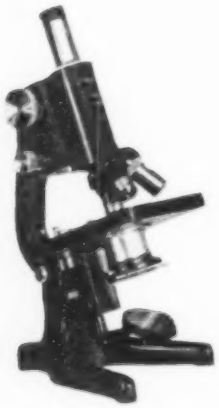

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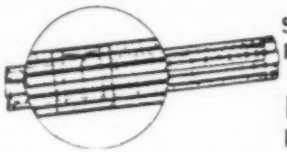

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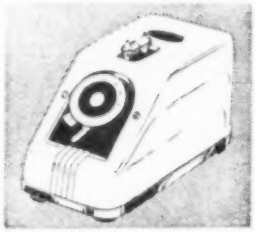

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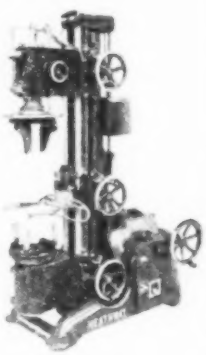

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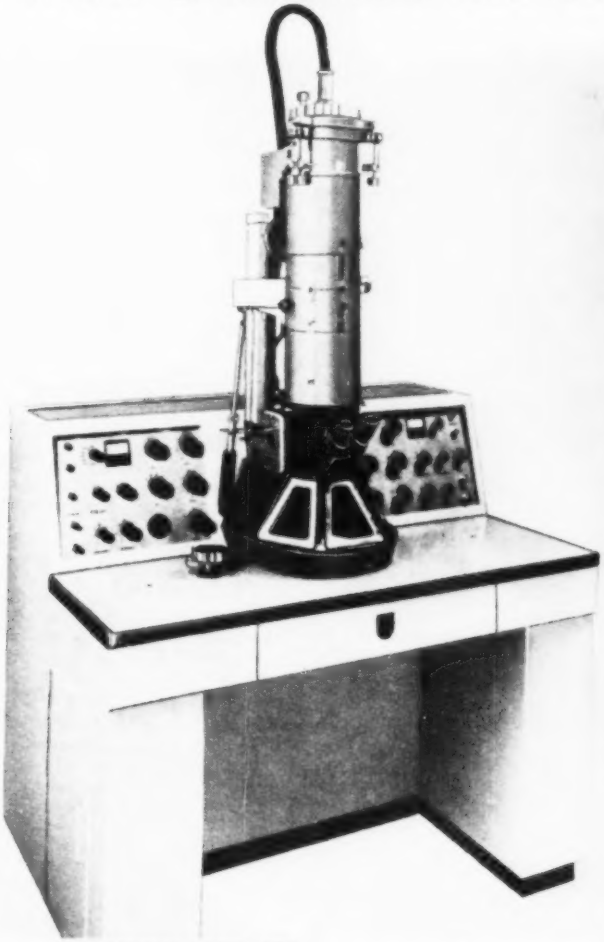

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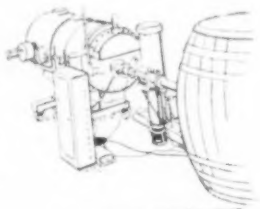
Subcritical Assemblies

Campbell[1], using a pulsed deuteron beam from a Van de Graaff® accelerator, has investigated the multiplicative properties of a water-U^{235} assembly. The dependence of thermal neutron lifetime on physical dimensions was measured and was found to agree with theory, with a reasonable allowance being made for the age to reach thermal energies.

Borst[2], using a 2-Mev Van de Graaff with the Be^9 (d, n) reaction, obtained an output of about 5×10^{10} neutrons per second and a neutron multiplication of 6.7 in a water-moderated "pickle barrel". The assembly had a criticality factor of 0.85. With the high neutron output from the Van de Graaff, it is possible to carry out lifetime studies of prompt and delayed neutrons, measurements of the effect of impurity in the water moderator and the effect of control rods on the criticality factor, measurements of cross-sections, and many other experiments concerned with neutron physics.



Van de Graaff pulsed-neutron source with subcritical assembly

Sjorstrand[3] of Sweden has reported measurements on a subcritical heavy-water reactor using pulsed neutrons. By this method it was possible to determine the criticality per unit volume of moderator and the effect of control-rod geometry on criticality. The overall criticality of the reactor could be measured each time some operating parameter was changed.

Pulsed Neutron Sources for Teaching

The ability to demonstrate some of the properties of the neutron can be invaluable in teaching. Experiments related to lectures can be designed to show neutron moderation with foils or other types of detectors. This can lead to a discussion of neutron diffusion and capture, and of the effects of different buckling factors and types of moderators. The addition of impurities to the water will alter the mean life, and the capture cross-sections for the impurities can be calculated and compared with other methods of measurement. The multiplicative properties of the assembly and the effect of control rods on the multiplication factor can be ascertained. *Thus the student can be shown all the steps in the design and operation of a full scale reactor — with a relatively simple piece of equipment.* The equipment investment is modest and the Division of Reactor Development of the U.S.A.E.C. has indicated willingness to support the purchase of the necessary equipment for colleges and universities.*

The sub-critical assembly can be used for group studies with adequate control for beginning students, but it is by no means limited to this type of teaching. The advanced student can use this device to carry out many important measurements of a fundamental nature which are needed by the reactor designers of today. Many of the gaps in our knowledge of reactor neutron theory can be filled through the use of this type of equipment.

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References:
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2. I. B. Borst — Nucleonics Aug. 1956, Vol. 14, No. 8, Pg. 60-68.
3. N. G. Sjorstrand — Vol. 5, 52, National Conference on Peaceful Uses of Atomic Energy — Geneva, 1955 — P/580.

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LETTERS TO THE EDITORS

PHYSICS

Glass Formation in Solutions of Hydrogen Peroxide–Water and Deuterium Peroxide–Heavy Water

We have found that if a hydrogen peroxide–water solution, of suitable concentration, is put into a tube and frozen extremely quickly by plunging the tube into a Dewar flask containing liquid oxygen (90° K.), a transparent colourless solid is formed. This solid has the properties of a glass, in that it is both transparent and amorphous. A glass is also formed if the hydrogen peroxide solution is allowed to fall as drops on to liquid oxygen.

The hydrogen peroxide used was high-test unstabilized hydrogen peroxide from Laporte Chemicals, Ltd. The various concentrations were made, either by mixing the standard concentrations supplied by Laporte or by dilution of approximately 95 per cent w/w hydrogen peroxide with laboratory-distilled water. No attempt was made to de-gas the solutions. When necessary, the hydrogen peroxide concentrations were checked by potassium permanganate titrations, and these were accurate to 1 per cent.

The most convenient method of testing whether a given concentration forms a glass or not was found to be that described by Livingston and Zeldes[1]. The liquid solution at room temperature was allowed to fall as drops, of 2–5 mm. diameter, on to the surface of liquid oxygen. Initially, the drop floated on the surface of the liquid and froze to form a sphere. For concentrations 45·5–87 per cent w/w, perfectly transparent glass spheres were formed; for all other concentrations, opaque white spheres were formed, and these were presumably polycrystalline.

A glass is again obtained when hydrogen peroxide, of 45·5–87 per cent w/w, is put into a glass tube, on to an aluminium plate or between glass plates and then frozen in liquid oxygen. The glass now, however, has very marked cracks. The formation of cracks is presumably due to thermal contraction. No cracks were found in the case of the spheres, since there are no constraining walls on the sample. For all samples the glass is completely stable and no transformations were found on storing at 90° K. for two days.

The boundary at 45·5 per cent w/w between the concentrations which produce polycrystalline material and those which produce a glass is very sharp and corresponds to the eutectic point (Banfield, R. H., private communication) at 45·3 per cent w/w. The boundary at 87 per cent w/w is far less marked and can vary by ± 5 per cent w/w; this concentration is well above the second eutectic point (Banfield, R. H., private communication) of 60·5 per cent w/w, but it coincides, however, with a well-marked change in the slope of the melting point/concentration curve for hydrogen peroxide–water solutions as determined by Giguère and Maass[2] and by Kubaschewski and Weber[3] from measurements on quickly frozen (non-equilibrium) solutions.

Cooper and Watkinson[4] made measurements on the supercooling of hydrogen peroxide–water solutions, using slow cooling. They found supercooling for concentrations between 50 per cent w/w and 97 per cent w/w (the highest concentration used); at 86 per cent w/w they recorded the lowest freezing temperature for supercooled liquid. Cooper and Watkinson also reported the formation of a glass at 86 per cent w/w, when the sample at 194·5° K. was transferred to liquid nitrogen (77° K.). Bolz, Mauer and Peiser[5] performed X-ray diffraction studies on 90–95 per cent w/w hydrogen peroxide (Mauer, F. A., private communication) condensed from the vapour at 77° K. For temperatures below 92° K. they found an amorphous glass giving very broad (8°) diffraction lines.

We have also studied the effect of warming the glass samples. The solution to be tested was put into a small test-tube holding about 5 ml. of solution. A thermocouple was put into the centre of the solution and the whole assembly plunged into liquid oxygen; a glass was formed with some cracks. The leads of the thermocouple were connected to a potentiometric pen recorder of 1 sec. response-time. The accuracy of temperature measurement was ± 2° K. The tube was removed from the liquid oxygen and was placed in the air at room temperature. A typical warming curve is shown in Fig. 1 for 61·0 per cent w/w hydrogen peroxide. The quick rise of temperature *AB* is associated with the appearance of opacity in the sample which spreads along the tube, and this is presumably due to exothermic crystallization of the solution. Several measurements were made on 61·0 per cent w/w samples, and for these it was found that crystallization occurred at 165 ± 6° K. Similar behaviour was found by Bolz, Mauer and Peiser[5], the crystallization for 90·95 per cent w/w hydrogen peroxide, however, commencing at 92° K. The region over which the temperature remains constant, *CD* in Fig. 1, is due to melting of the crystals and was found to be at 217 ± 2° K. This is in agreement

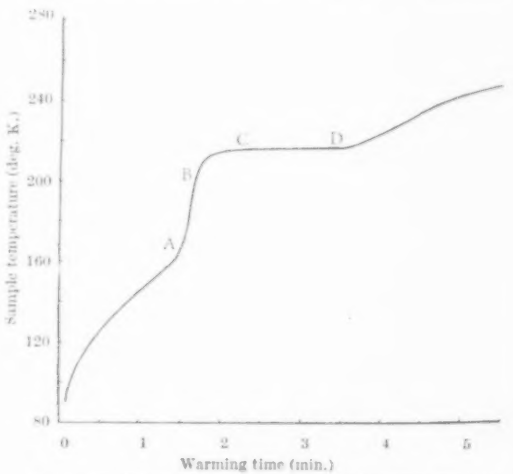

Fig. 1. Warming curve for 61·0 per cent w/w hydrogen peroxide

with measurements of the melting points by Giguère and Maass[2], and by Kubaschewski and Weber[3]. We have tested two other concentrations, 45·5 per cent w/w and 80 per cent w/w a these showed a similar behaviour, crystallization taking place at 141 ± 10° K. and 157 ± 10° K. respectively. The melting points of these two concentrations were found to be 222 ± 5° K. and 215 ± 5° K., in agreement with published measurements[2,3]. In all the glass samples the cracks annealed out between 130 and 155° K., that is, before the crystallization took place.

Tests of glass formation were also made using deuterium peroxide, obtained from Laval University. The concentration used was 80 per cent w/w, with 99 per cent deuterium. It was found that a stable glass was produced as above, both in spheres and in a glass tube. Giguère and Secco[6] have also reported the formation of glasses in deuterium peroxide, but on storing in liquid air for 10 min. they found a spontaneous conversion to crystallization. We have not found this effect and cannot explain the difference between the two results.

These observations were obtained during experiments involving ultra-violet irradiation of hydrogen peroxide–water solutions at 90° K. for electron spin resonance spectroscopy[7].

The potassium permanganate titrations were performed by Mr. J. M. Richards of this Department. We wish to acknowledge helpful discussions with Mr. R. H. Banfield of Laporte Chemicals, Ltd., and, in particular, for his suggestion of an examination of the eutectic mixtures. The hydrogen peroxide for these measurements was kindly supplied by Laporte Chemicals, Ltd. The deuterium peroxide was given to us by Prof. P. A. Giguère of Laval University, Quebec. This work was supported by the British Empire Cancer Campaign, for the assistance of which we express grateful thanks.

Robert C. Smith
S. J. Wyard

Department of Physics,
Guy's Hospital Medical School,
London.

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A Spectrometer for the Far Infra-red

A spectrometer based on a Fresnel zone plate as the focusing and dispersing element has been constructed for use with infra-red radiation between 35μ and 80 c.

The instrument is intrinsically simple. A heated nichrome coil and a Fresnel zone plate are mounted on opposite ends of a 4-m. *I*-beam so that the zone plate produces a series of monochromatic images of the source disposed along the axis of the instrument. A bolometer detector mounted on a carriage moves along a straight track attached to the *I*-beam so as to scan the spectrum. A light chopper in front of the source uses alternating open holes and potassium bromide windows to eliminate virtually all but first-order spectra from the signal. The sample cell is located in the light path close to the source.

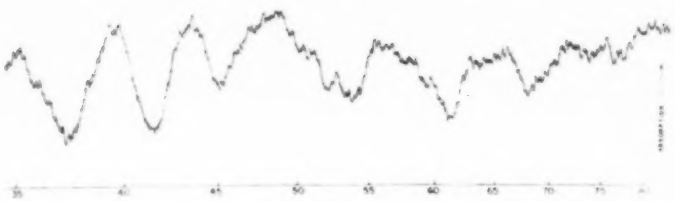

Fig. 1

The zone plate is of the reflecting type, containing 234 half-wave Fresnel zones. The surfaces of the even-numbered zones are raised 12·5μ above those of the odd-numbered zones to give a maximum optical efficiency at 50μ. The zone radii are calculated to make the system free from spherical aberration at 68μ and to give the zone plate a focal length of 73·5 cm. at that wave-length.

The zone plate focuses a monochromatic image of the source directly on the bolometer element with no intervening collimating mirrors, or movable slits, as in a grating spectrometer. The simplicity of this design leads to ease of construction and good light-gathering power. Fig. 1 shows the absorption spectrum of atmospheric water vapour.

Patents have been applied for.

We wish to thank the Trans Mountain Oil Pipe Line Co. and its president, Dr. D. M. Morrison, for a grant which made possible the construction of this instrument.

R. H. Wright
P. N. Daykin

British Columbia Research Council,
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Elimination of a Glow Discharge in an Induction-heated Vacuum Furnace

Recently, J. P. Burden[1] discussed the elimination of a glow discharge in induction-heated vacuum furnaces. As Burden indicated, the glow discharge is troublesome because it robs energy. In addition, in vacuum analysis systems, the discharge is often intolerable because of the consequent evolution of gases from glass furnace parts.

For the past three years, an almost perfect method of eliminating the glow discharge has been employed in this Laboratory. It was found that a small horseshoe permanent magnet placed near the glass furnace wall prevents the initiation of a discharge, or immediately quenches a discharge once started. The exact position of the magnet varies slightly, and must be determined empirically, but is about one centimetre or less from the furnace wall. The system to which the magnet 'trick' has been applied is a conventional vacuum fusion analysis apparatus with an all-glass, air-cooled furnace[2] inductively heated by a 2·5-kW., 500-kc. oscillator. The idea of using a magnet in the manner indicated was suggested by the common

application of a permanent magnet as an 'ion trap' on television picture tubes.

Strangely enough, the use of the magnet has twice been observed to have the opposite of the desired effect. That is, a glow discharge was initiated when the magnet was brought near the furnace, and extinguished on removal of the magnet.

No attempt will here be made to suggest how the magnet succeeds (or rarely, does not succeed) in eliminating a glow discharge. Suffice it to say that the success has been just short of perfection, and the more gratifying because it was attained at little expense and much convenience.

JOHN E. FAGEL

Refractory Metals Laboratory,
General Electric Company,
Cleveland,
Ohio.

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Visible Twist on Sodium Chloride Whiskers

IT is well known from Eshelby's[1] work that a whisker containing an axial screw dislocation will have the form of a twisted rod. Sodium chloride whiskers have been grown in which such a twist was quite visible to the naked eye.

The whiskers were prepared by a modification of Evans's method[2]. A small sodium chloride crystal grown from the melt was placed in a solution of sodium chloride, containing a small amount of polyvinyl alcohol. The whiskers grew on this seed-crystal. The mean length of the whiskers was 150 mm., their thickness 1–30μ and they were rectangular in cross-section. Some of the whiskers, mainly the thinner ones, were spiral. The twisted form was easily visible to the naked eye: with suitable light brighter and darker spots became visible along the lengths of whiskers, because due to their twisted form only some parts of them reflected the light. The distances between light spots on most of the crystals were 1–40 mm. and they were uniformly distributed along the length of the whiskers. It is suggested that this is probably a twist described by Eshelby. He gives the formula for the twist per unit length as follows:

$$\text{twist } \alpha = k \times \frac{\text{Burgers vector } b}{\text{area of whisker cross-section } A}$$

where k is a constant depending on the shape of the cross-section. The Burgers vector of the screw dislocation calculated with this formula results in values of 60–240 Å. These are the results of measurements carried out on twelve whiskers. Webb[3] obtained similar results among others by the X-ray diffraction method.

In our opinion, polyvinyl alcohol plays little part in the production of whiskers, because Gyulai[4] also found spiral whiskers in aqueous solution of potassium bromide containing no polyvinyl alcohol. The whiskers were tested by twisting. Fig. 1*a* shows a spiral whisker having eleven light-spots. The same whisker is shown in Fig. 1*b*, twisted outwards through 360°. It can be seen that the number of light-spots has diminished by four. Twisting further through 360°, the number of light-spots diminished to three (Fig. 1*c*). Twisting the whisker through 990°, it became quite smooth, and light-spots were no longer

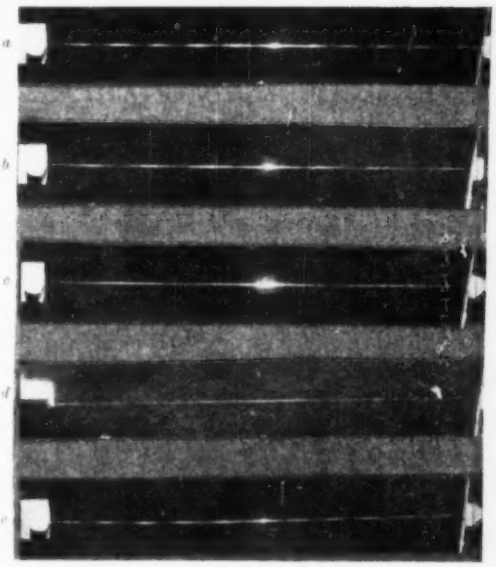

Fig. 1. *a*, Naturally twisted sodium chloride whisker (original length); *b*, the same whisker twisted through 360°; *c*, the same whisker twisted through 720°; *d*, the same whisker twisted through 990°; *e*, the same whisker, one of its ends cut off after twisting, and the whisker quite twisted back

visible (Fig. 1*d*). If one end is cut the whisker twists back again. After this twisting-out the twisting-back phenomenon was observed in each test. In most cases the whisker was almost completely twisted back. It appears that this phenomenon disagrees with Eshelby's suggestion, according to which after a certain twisting the dislocation leaves the whisker. There may be several explanations.

Further investigations on whiskers are in progress. A detailed paper will be published in *Acta Physica Hungarica*.

We wish to thank Prof. Z. Gyulai for valuable discussion and interest.

B. JESZENSZKY
E. HARTMANN

Institute of Experimental Physics,
Technical University,
Budapest.

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Weissenberg Effect in the Thick White of the Hen's Egg

WHEN a vertical rod is rotated in certain liquids, the liquid climbs up the rod. This phenomenon was apparently first observed by Weissenberg and Russell[1], and in 1949 Reiner, Scott Blair and Hawley[2] suggested that it be described as the 'Weissenberg effect'.

Its theory is not clear and has been discussed by Garner and Nissan[3], Rivlin[4], Reiner *et al.*[5] and Roberts[5]. The effect occurs only rarely and has

been observed in highly viscous solutions of rubber in benzene[3], certain soaps in hydrocarbon solvents[3], over-aged sweetened condensed milk[3] and certain types of dilatant honey[4].

During an investigation into the rheological behaviour of cake batters it was found that most of them exhibited the Weissenberg effect to a greater or lesser extent dependent on their egg content. When the separate constituents of egg were tested it was apparent that the more viscous component of the albumen, the so-called thick white[7], sometimes also referred to as the middle dense layer or albuminous sac[8], exhibited the Weissenberg effect most markedly. This material was readily isolated by a method virtually identical with that of Brooks and Hale[7]. The eggs were broken individually on a clean B.S. 14 mesh sieve which had been wetted with water and the outer thin white was allowed to drain off. After tilting the sieve gently to and fro for 1 min., the white around the yolk was cut and the yolk removed by hand. After draining off the inner thin white, the thick white remained on the sieve and could be used for the test.

The thick white of the hen's egg thus provides an easily accessible material by means of which the Weissenberg effect may be demonstrated.

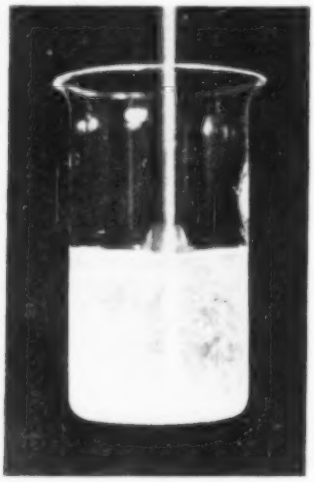

Fig. 1

I wish to thank Mr. A. W. Hartley for Fig. 1, which shows the Weissenberg effect in the thick white.

H. G. Muller

Spillers, Limited,
Technological Research Station,
Station Road,
Cambridge.

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GEOPHYSICS

Lunar Tide in the F_2 Layer of the Ionosphere near the Geomagnetic Equator

It is well known that the maximum in the lunar tide variation of f_0F_2 occurs at about 10 lunar hours at moderate geomagnetic latitudes and at about 04 lunar hours near the geomagnetic equator[1,2]. Recent analyses of the lunar variations at Singapore, Ibadan and Bombay have indicated non-agreement in the phases of the variation at stations having the same geomagnetic latitudes.

In this communication the analysis of lunar variations of f_0F_2 at Leopoldville for the period of three years from November 1953 to October 1956 is presented. From the published hourly values of f_0F_2, daily averages of three-hourly values between 11 hr. to 13 hr. (15° E.M.T.) are computed and are referred to as midday values. The 27-day running averages of these values are computed and are subtracted from the individual day values for the central day of the respective 27-day period to obtain the deviation of f_0F_2 for that day. The deviations of f_0F_2 for days having the same phase (μ) of the Moon are then grouped together, and thus 24 such groups are obtained for the different phases of the Moon. The average deviations of f_0F_2 for each phase are computed separately for the months of southern solstice (November, December, January and February), for equinoxes (March, April, September and October), for the northern solstice (May, June, July and August) as well as for the whole year. To avoid the effects of

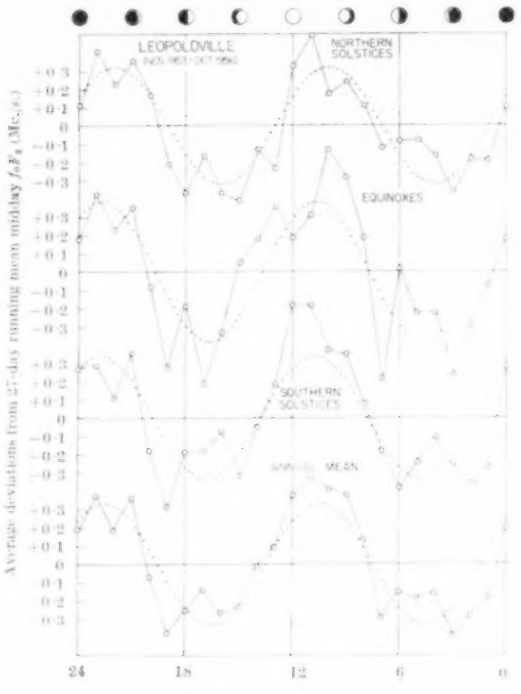

Fig. 1

Table 1. Amplitude P_2 and Phase t_2 of the Lunar Variation of Noon f_0F_2 at Low Latitude Stations

Station	Geomagnetic latitude	Magnetic latitude	P_2 (Mc./s.)	t_2 lunar hour	Reference
Huancayo	0·6° S.	0°	0·45	4·0	1
Leyte	0·2° S.	3° N.	0·53	4·2	1
Tiruchy	1° N.	2·5° N.	0·13	2·8	1
Christmas Islands	2·1° N.	2·5° N.	0·33	4·7	1
Madras	3·1° N.	5·5° N.	0·14	3·8	2
Ibadan	10·4° N.	2·5° S.	0·33	3·3	4
Singapore	10·6° S.	8° S.	(0·30)	(4·0)	3
Leopoldville	3·1° S.	19° S.	0·33	10·5	this communication
Bombay	9·8° N.	12·5° N.	0·24	10·0	2
Ahmedabad	13·6° N.	18·6° N.	0·35	10·2	2
Trinidad	22° N.	23·5° N.	0·31	9·2	1
Manil	20·9° N.	21·5° N.	0·36	9·1	1

the magnetic disturbances, the days with A_p value greater than 50 were excluded in averaging. Further, to reduce the scatter, the deviations exceeding more than 20 per cent of the corresponding 27-day mean value were also excluded. These eliminated only less than 9 per cent of the total number of available values. The result of the analysis is shown in Fig. 1. It may be mentioned that from one day to the next μ decreases by 0·81272, and the lunar time corresponding to a phase μ is given by $\mu \pm 12$ (lunar hours).

In Table 1 are compared the amplitudes and phases of the lunar variations of f_0F_2 at Leopoldville and at a number of low-latitude stations in the world. It is seen that the lunar variation at Leopoldville (geom. lat. $\Phi = 3{\cdot}1°$ S.) is completely out of phase with that at Madras ($\Phi = 3{\cdot}1°$ N.) or at any other equatorial station. The phase of the lunar variation at Leopoldville (magn. lat. = 19° S.) is very nearly the same as that at Ahmedabad (magn. lat. = 19° N.) having the same magnetic latitude. This suggests that the stations having the same magnetic latitude rather than the same geomagnetic latitude experience similar variation of f_0F_2. The equatorial type of lunar variation at Ibadan and the middle latitude type of variation at Bombay in spite of the geomagnetic latitudes of both stations being about 10° can be understood if one considers that the magnetic latitudes of the stations are about 3° S. and 13° N. respectively. The reversal of phase of the lunar tide in f_0F_2 takes place around magnetic latitude 10° or at magnetic dip 20°.

R. G. Rastogi*

Radio and Electrical Engineering Division,
National Research Council,
Ottawa.

* Present address: High Altitude Observatory, University of Colorado, Boulder, Colorado.

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Spread-*F* and the Latitude Variation of Occurrence of Whistlers

Recent work of whistling atmospherics has suggested that the incidence of the phenomenon is dependent on latitude. Crouchley[1], using data from Australian and Japanese stations, demonstrated that whistler activity reaches a maximum at about 45° geomagnetic latitude, while the Stanford group[2] report a maximum of occurrence at 50° geomagnetic latitude. In both these reports a marked decrease in activity at lower and higher latitudes is noted. The decreasing incidence at higher latitudes has been attributed[3] to decreasing thunderstorm activity, and rapidly increasing path-length and absorption with increasing latitude. However, the fall-off in activity at low latitudes cannot be so explained. Smith, Helliwell and Yabroff[3] have suggested an explanation of this low-latitude fall-off in terms of whistler propagation within field-aligned ducts. They showed that the necessary ionization enhancement within the ducts for *F*-layer heights falls off markedly with increasing latitude and argue, therefore, that this suggests that whistler occurrence should increase with latitude, since large enhancements would be expected to occur less frequently than small enhancements. It is the purpose of this communication to examine this point in more detail.

The frequency-spreading component of spread-*F* has been interpreted[4,5] as being due to the availability of a range of values of $N_{max.}$ at the maximum of the F_2 layer; this range of values is thought to correspond to a system of irregularities each involving an enhancement (or a deficiency) of electron density relative to the background ionization. For any particular occurrence of frequency-spreading it is possible, in terms of this hypothesis and assuming critical reflexion conditions to apply, to calculate the ionization enhancement ($\Delta N/N$) required. It is now suggested that these postulated irregularities in the F_2-layer are, in fact, the lower extremities of the whistler ducts. If this is the case, then estimates of the electron density enhancements obtained from frequency-spreading information should support the contention of Smith *et al.* outlined above.

In work to be published elsewhere I have been able to fix limits to the range of values of ΔN observed at seven stations spread in geomagnetic latitude. Combining this information for a typical winter month with the monthly median critical frequency, it has been possible to produce, as shown in Fig. 1, a diagrammatic representation (shaded strip) of how the range of values of $\Delta N/N$ varies with geomagnetic latitude. (The position of that portion of the shaded strip bounded by dashed lines is less certain than

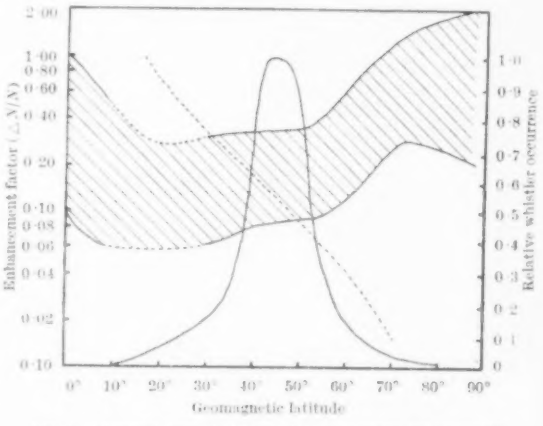

Fig. 1. Observed irregularity of electron density enhancement factors (shaded area) compared with the minimum required for whistler duct propagation (dashed curve) and with whistler occurrence data (full-line curve) for a range of geomagnetic latitudes

elsewhere because of the low incidence of frequency spreading at these latitudes.) Also shown in Fig. 1 is the graph of minimum $\Delta N/N$ against geomagnetic latitude (dashed curve) due to Smith *et al.* and Crouchley's latitude distribution of whistler occurrence. (Since whistler activity is most pronounced in the winter months the latitude distribution of whistler activity is largely dependent upon winter conditions.) It will be noted that for latitudes less than about 30° the observed range of $\Delta N/N$ involves values considerably less than the values required by Smith *et al.* and that this corresponds to the region of low whistler occurrence. At 32° the largest observed value of $\Delta N/N$ corresponds to the minimum required for whistler propagation, while above 50° all the observed values of $\Delta N/N$ are of sufficient magnitude to support whistler propagation. The 30–50° latitude region corresponds to that in which the whistler activity increases. It seems, therefore, that the explanation of the latitude variation of whistler activity based on propagation within field-aligned ducts is consistent with ideas at present being used to interpret the frequency-spreading component of spread-*F*.

I am indebted to Mr. J. Crouchley and Dr. J. A. Thomas for their interest and helpful discussion.

D. G. Singleton

Physics Department,
University of Queensland,
Brisbane.

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METALLURGY

Micropitting of Titanium during Anodic Oxidation in Formic Acid

The anodic oxidation of titanium in the majority of electrolytes (sulphuric, phosphoric, boric acid, etc.) results in the formation of a thin homogeneous dielectric oxide film of titanium dioxide (amorphous or crystalline). At constant current the potential increases with increasing film thickness, and, if the potential is then maintained constant, the ionic current decreases rapidly and the current becomes almost entirely electronic. In these circumstances, providing film breakdown does not occur, film growth practically ceases and oxygen evolution becomes the predominant electrode process.

In chloride electrolytes, however, film growth proceeds up to a potential of ~ 12–14 V., and if the potential is increased above this value film breakdown occurs, and titanium ions pass into the electrolyte, and are then precipitated as titanium dioxide. Corrosion of the titanium is confined to a relatively few, widely dispersed, small areas of the metal surface with the consequent formation of gross pits while the rest of the surface, which is coated with the initially formed anodic oxide, remains passive.

During a study of the anodic oxidation of titanium in various electrolytes it has been found that formic acid (and formates) gives rise to a phenomenon which does not appear to have been reported previously. Within a certain range of temperature and concentration of formic acid (Fig. 1, zone *C*) film formation,

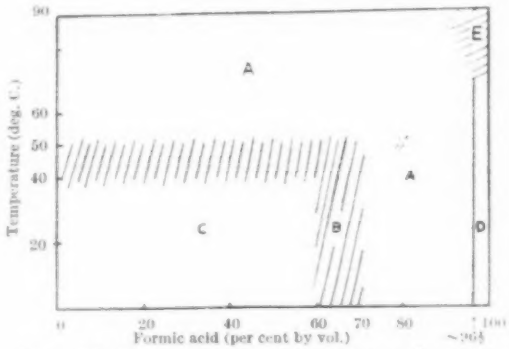

Fig. 1. Effect of concentration and temperature on the anodic behaviour of titanium in formic acid. *A*, Homogeneous dielectric oxide films; *B*, transition zone where homogeneous films show evidence of micropitting; *C*, micropitting; *D*, thick yellow non-adherent oxide films; *E*, transition zone between *A* and *D*

at constant current, proceeds up to a voltage of ~ 60 V., but as the potential increases above this value, very fine pits are formed uniformly over the metal surface (micropitting) and simultaneously titanium oxide is precipitated from the electrolyte. The potential slowly increases to ~ 120 V., indicating film growth, and then remains practically constant, and if anodizing is continued the pits are propagated into the metal to a considerable depth (Fig. 2). A microscopical examination of the metal surface during the initial stages of micropitting has revealed that different areas on the metal surface have different interference colours showing that the thickness of the surface oxide is not uniform.

If, however, the temperature of the electrolyte is greater than ~ 50° C. or if the concentration is in the range of ~ 70–96 per cent by vol. formic acid (Fig. 1, zone *A*) micropitting does not occur and a homogeneous dielectric oxide film is formed. It should be observed that at 25° C., at a concentration of ~ 96 per cent formic acid, film formation can proceed to 400 V. without film breakdown, whereas in boric acid the maximum formation voltage is only ~ 250 V.

In region *D*, at very high concentrations of formic acid (~ 96·5 per cent to concentrated), a thick

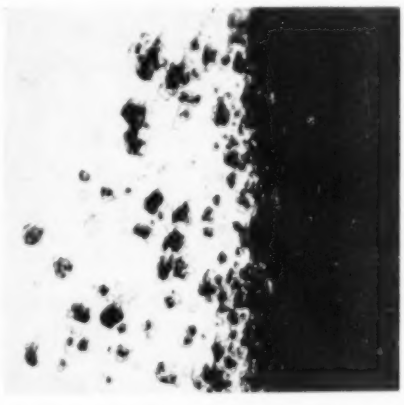

Fig. 2. Section of a micropitted specimen produced using 1 per cent by vol. formic acid, 25° C., 5 m.amp./cm.^{2} for 4 hr. (× c. 66). The section has been cut at 5° to the surface to exaggerate depth of penetration of pits. Depth of penetration, $4·5 \times 10^{-3}$ cm.

dark-yellow, non-adherent oxide forms on the metal surface.

A consideration of data[1] on the rate of corrosion in different concentrations of formic acid at 35° C. reveals that zone *C* corresponds to the range of concentration where the corrosion-rate is high and region *A* where the corrosion-rate is at a minimum.

It is apparent that the mechanism of micropitting is highly complex, as the electrode processes which occur involve the anodic oxidation of titanium, localized corrosion of titanium, oxidation of formic acid to carbon monoxide and dioxide and oxidation of hydroxyl to oxygen. The heterogeneity of the metal and adsorption of formic acid on active centres[2,3] and the formation of complexes between titanium and formic acid may also contribute to the overall process.

The reason for the formation of barrier films at more elevated temperatures and at higher acid concentrations (Fig. 1, zone *A*) may involve a consideration of the kinetics of oxidation of formic acid and the properties of the anodic oxide film under the conditions specified.

The phenomenon of micropitting appears to be confined to the titanium–formic acid system as similar results could not be achieved with niobium or zirconium.

It is considered that further work on this phenomenon may contribute to an understanding of the general mechanism of the pitting corrosion of metals.

The anodizing of titanium in formic acid to produce a micropitted surface as an aid to anti-galling, lubrication and adhesion of surface coatings is covered by a patent application[4] made by the National Research Development Corporation.

R. A. Piggott
L. L. Shreir

Metallurgy Department,
Battersea College of Technology,
London, S.W.11.

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Some New Intermetallic Compounds of Thorium of the Type Th_7X_3

As part of an investigation of the constitution of alloys of thorium with the metals ruthenium, rhodium, palladium, osmium, iridium and platinum, a series of 1-gm. samples of alloys containing up to 33 atomic per cent of each precious metal was prepared by arc-melting the component materials in a zirconium-gettered argon atmosphere, weight losses on melting being negligible. Metallographic and X-ray results on as-cast and on annealed material suggest that the intermetallic compounds richest in thorium are: Th_7Ru_3, Th_7Rh_3, Th_7Pd, Th_7Os_3, Th_7Ir_3 and Th_7Pt_3. Each compound forms a eutectic with thorium and the composition and temperature of these eutectics are given in Table 1. The solid solubility of each metal in thorium and the age-hardening behaviour of thorium-rich alloys have also been investigated.

Alloys corresponding to the five compounds, Th_7X_3, were brittle and powders for X-ray studies were prepared by crushing in air; powder patterns were obtained with a Guinier-type focusing camera using monochromatized copper radiation. These X-ray

Table 1

System	Phases in the eutectic	Composition of the eutectic (percentage of precious metal)	Melting point of the eutectic (deg. C.)
Th – Ru	Th + Th_7Ru_3	16 ± 1	1,262 ± 12
Th – Rh	Th + Th_7Rh_3	20 ± 1	1,237 ± 12
Th – Pd	Th + Th_7Pd	22 ± 1	1,112 ± 12
Th – Os	Th + Th_7Os_3	14 ± 1	1,287 ± 12
Th – Ir	Th + Th_7Ir_3	15 ± 1	> 1,300
Th – Pt	Th + Th_7Pt_3	17·5 ± 0·5	1,242 ± 12

Table 2

Compound	'a' (Å.)	'c' (Å.)	c/a	X-ray density (gm./c.c.)
Th_7Ru_3	9·969	6·302	0·632	11·82
Th_7Rh_3	10·031	6·287	0·627	11·71
Th_7Os_3	10·031	6·296	0·628	13·27
Th_7Ir_3	10·076	6·296	0·625	13·40
Th_7Pt_3	10·126	6·346	0·627	13·01

films were indexed on the basis of a hexagonal lattice, systematic extinctions of the $h\,h\,\overline{2h}\,l$ reflexions were noted when l was odd and the observed intensities show good agreement with those for the Th_7Fe_3 structure, space group $C^4_{6v} - P\,6_3mc$. Lattice parameters, axial ratios and X-ray densities for the new compounds are given in Table 2.

Grateful acknowledgment is made to Prof. J. G. Ball under whose supervision this work was carried out, and also to the Atomic Energy Research Establishment, Harwell, for financial support and for allowing me to make use of some experimental facilities.

J. R. Thomson*

Department of Metallurgy,
Imperial College of Science and Technology,
London, S.W.7.

* Formerly J. R. Murray.

CRYSTALLOGRAPHY

X-Ray Correlation of the *A-B* Layer Order of Cadmium Selenide with the Sign of the Polar Axis

Cadmium selenide (CdSe) is typical of the hexagonal semiconducting compounds formed from elements of Group II and Group VI of the Periodic Table. It possesses the wurtzite structure and contains a unique polar axis (the *c*-axis). Compression along this axis produces opposite electric charges on the basal faces, which also differ in their response to etching and in other properties. An examination of the crystal structure as shown in Fig. 1 shows the polarity clearly. Viewed normal to the *c*-axis, pairs of closely spaced cadmium–selenium layers are seen. The 'cadmium side' and the 'selenium side' are defined in Fig. 1.

For an understanding of the polar physical and chemical effects it is important to know which is the cadmium and which is the selenium side of the *c*-axis. It is possible to make such an identification by observing the effects of anomalous X-ray dispersion on the intensity of the X-rays reflected from the positive and negative sides of the basal planes (00.*l*) and (00.$\bar{l}$). Previous workers have investigated cubic zinc sulphide, gallium arsenide and indium arsenide in such a manner[1–3]. To our knowledge, this communication reports the first application of this

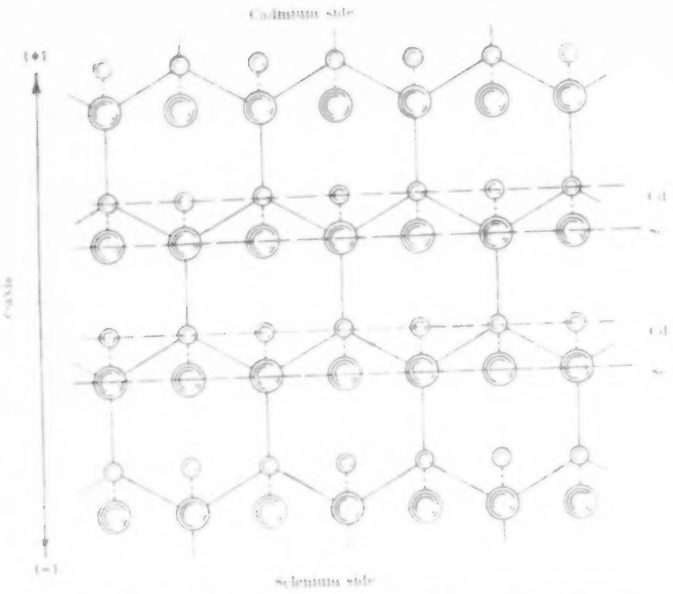

Fig. 1. Alternate layers of cadmium and selenium parallel to the (00.1) surfaces

technique to a wurtzite structure. By making dispersion corrections to the atomic scattering factor, the structure factor ratio $\frac{|F(00.l)|^2}{|F(00.\bar{l})|^2}$ (which is proportional to the ratio of the integrated intensities) can be calculated[1]. These theoretical ratios calculated for copper $K\alpha$ radiation are shown in Table 1.

Table 1. Rotated Integrated Intensity Ratios

Plane	Theoretical intensity ratio $\frac{\|F(00.l)\|^2}{\|F(00.\bar{l})\|^2}$	Observed intensity ratio
00.2	0·869	0·862
00.4	1·000	0·973
00.6	1·225	1·241
00.8	1·000	1·045

The experimental procedure is quite exacting. A circular plate of cadmium selenide, the surface of which was orientated to within 3 min. of arc with the (00.1) plane, was etched and given an optical polish with 0·3μ alumina. Measurements with an optical flat indicate that both surfaces were slightly rounded but were flat to 10 fringes. Next, the disk was placed on a bed of wax in a cylinder which was inserted into the rotating flat specimen spinner of a standard 'Norelco' diffractometer. The polished crystal was pushed up against an optical flat which was held against the top surface of the specimen holder. When the interference rings were centred, the crystal was locked into position. To test the parallelism of the crystal surface with the plane of the specimen holder, the latter was rotated by motor while a distant light source was reflected off the rotating crystal surface. The steadiness of this optical image proved to be an extremely sensitive test of the line-up. The experimental values for the integrated intensities were obtained by counting while simultaneously rotating the crystal at 77 r.p.m. and slowly scanning the entire peak at 1/8° (2θ) per min. After the rotated integrated intensities were measured on one side, the crystal was turned over, aligned, and the same process was repeated (care being taken that all conditions were identical for any two (00.l) (00.$\bar{l}$) reflexions). For different peaks various aluminium filters were used so that the counting-rate fell within the linear response range of the scintillation counter. Table 1 compares a typical set of results with the corresponding theoretical values.

The side of the crystal proved to be the cadmium side by the X-ray data of Table 1 was found to become positively charged on extension. By the sign convention of the I.R.E. 1949 Standard on Piezoelectricity the + end is therefore the outward directed normal from the cadmium side.

Having established this correlation, other differentiating properties of opposite (00.1) surfaces which have been correlated to the piezoelectric sign can also be related to the A–B layer order. Table 2 is a tabulation of some of these correlations for cadmium selenide.

Considering the similar character of all wurtzite and sphalerite compounds, it would appear reasonable for these compounds to show the same type of correlation as cadmium selenide, namely, the more metallic layer will be in the +c direction, as defined by the piezoelectric sign. This is in keeping with the findings for zinc sulphide and (by inference from the etching behaviour) for gallium arsenide and indium arsenide[1-3]. Any theory which attempts to explain the differentiating properties of the opposite (00.1) surfaces of wurtzite and the opposite (111) surfaces

Table 2. Correlation of A–B Layer Order with Other Properties which Distinguish the Opposite (00.1) Surfaces of Cadmium Selenide

Property	(00.1) surface. Outward normal to surface points in + c direction	(00.1) surface. Outward normal to surface points in − c direction
Sign of piezoelectricity on extension	(+) As defined by 1949 I.R.E. convention	(−)
A–B layer order	See Fig. 1	
Etching characteristics in aqua regia (excess selenium removed)	Shiny, symmetric pits bevelled edges. Equal or slower etch rate	Dull or cratered, no symmetry pits, no edge bevelling. Equal or faster etch rate
Relative sign of electrolytic solution potential 1 : 1 aqua regia	(+) More 'noble' by 50–70 mV.	(−)
Crystal habit at positive and negative ends	More complex pyramid development	Prominent face is the pedion. Pyramids small or absent

for sphalerite compounds must be compatible with these findings.

This work was supported by the U.S. Air Force, Wright Air Development Division.

R. Zare
W. R. Cook, jun.
L. R. Shiozawa

Clevite Corporation,
540 East 105 St.,
Cleveland 8,
Ohio.

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OCEANOGRAPHY

Organic Acids in Pacific Ocean Waters

Organic acids dissolved in waters of the Pacific Ocean were isolated by: (1) solvent extractions with carbon disulphide and chloroform, and (2) by co-precipitation with ferric hydroxide sols.

The solvent extractions were carried out on 15·3–20·0 l. of sea-water samples freed of particulate matter by filtration through '*HA* Millipore' filters (pore size: 0·45μ). The residues from chloroform and carbon disulphide extracts were methylated with methanol and a trace of concentrated sulphuric acid, and these products were then submitted to gas chromatographic analysis using an 'Aerograph' model 110-*C* gas chromatograph (Wilkens Instrument Co., Walnut Creek, California) incorporating 5- and 10-ft. Craig polyester succinate columns. The fatty acid esters isolated were identified by their retention times on the column with respect to known fatty acid esters and in the case of the methyl esters of palmitic and stearic acids by collection from the column and subsequent infra-red spectra. Table 1 lists the fatty acids isolated in μgm./l., and includes pertinent data on sample location and depth, extraction *p*H, and indicates the amounts of the unknown fatty acids C_x, C_y and C_z. From their infra-red spectra, C_x, C_y and C_z are indicated to be fatty acid esters. Their relative positions on the gas chromatographic traces gave retention times identical with the C_{15}, C_{17} and C_{19} normal, saturated fatty acid esters. Fig. 1 illustrates two representative traces for samples 47·A and 10·A.

To determine the percentage recovery of the fatty acids from sea-water a tracer experiment was run using palmitic acid-1-^{14}C (Nuclear-Chicago, Cat. No. *CFA*-23), added as 2,345 c.p.m. to each 2·40–2·48 l. sample of filtered sea-water prior to extraction with chloroform. The samples were acidified with hydrochloric acid to a *p*H of 2·0, and the solvent

Table 1. Fatty Acids isolated from Sea-water

Sample (1)	Location	Depth collected (m.)	Depth to bottom (m.)	Volume extracted (l.)	Extraction (*p*H)	μgm./l.															No. of major peaks (5)	Total μgm./l. (3)
						Saturated						Unsaturated Mono-		di-	Unknown			Miscellaneous				
						C_{13}	C_{14}	C_{16}	C_{18}	C_{20}	C_{22}	C_{14} (C—C)	C_{16} (C—C)	C_{18} (C—C_2)	C_x	C_y	C_z					
10·A	31° 40′ N. 119° 35′ W.	1,000	3,290	19·0	1·30	2·3	4·3	20·9	14·2	1·8	1·4	0·3	8·3	1·4	—	—	—	1·6 (4)	13	56·5
35·A•	32° 40′ N. 118° 09′ W.	1,290	2,020	18·1	3·10	0·4	1·8	14·6	22·2	8·1	tr.	—	—	—	6·6	15·5	14·1	6·4	14	89·7
47·A•	32° 40′ N. 118° 09′ W.	1,500	2,020	19·0	2·88	0·2	1·3	7·9	14·0	7·0	tr.	—	—	—	3·3	10·1	9·2	7·4	14	60·4
127·B	25° 19′ N. 114° 05′ W.	1,957	4,070	20·0	2·30	0·3	2·5	12·2	17·7	5·4	—	—	—	—	6·2	13·1	10·1	4·2	14	71·7
34·A	46° 46′ S. 123° 57′ W.	2,427	4,330	15·4	2·23	1·5	1·6	3·2	7·1	tr.	—	—	—	—	tr.	tr.	tr.	6·7	10	20·1
57·A	26° 45′ N. 123° 00′ W.	987	4,280	20·0	7·50	0·7	2·9	11·1	8·9	2·5	—	0·8	1·4	1·0	—	—	—	3·6	10	32·9
24·A	31° 41′ N. 119° 35′ W.	1,020	3,570	19·0	7·50	0·5	1·9	8·3	6·5	1·5	—	3·0	7·5	2·9	—	—	—	0·1	10	32·2
35·A	46° 46′ S. 123° 57′ W.	2,427	4,330	15·3	7·58	0·3	0·4	2·7				—	—	—	—	—	—	—	7	3·4
70? (2)	32° 40′ N. 118° 09′ W.	1,500	2,020	56	4·5	0·3	0·5	1·5	3·7	2·1	tr.	—	—	—	1·0	2·0	2·5	2·7	10	16·3

(1) Samples marked with asterisk were extracted with carbon disulphide; samples not marked, with chloroform.
(2) This sample had previously been precipitated with ferric hydroxide.
(3) These values represent minimum yields and are felt to be correct within a factor of two.
(4) Appears to be palmitolinoleic (hexadecadienoic) ester. Also shows indications of C_{15} and the unsaturated analogues of C_{18} and C_{16}.
(5) Identifiable peaks appearing on the gas chromatographic traces.

Table 2. Palmitic Acid-1-^{14}C Tracer Experiment

Sample (1)	Depth (m.)	Volume (l.)	Percentage of recovery free acid	Percentage of recovery methyl esters	Acids isolated as methyl esters (μgm./l. water) (3)							
					C_{12}	C_{14}	C_{16}	C_{18}	C_x (C—C)	C_y (C—C)	C_z (C—C_2)	Total
Control (2)	—	2·40	75·7	13·0	3·3	4·4	6·6	—	—	—	—	14·3
1	10	2·48	97·9	8·9	1·9	3·3	24·8	—	—	—	—	30·0
2	91	2·44	96·4	12·5	4·1	5·0	28·5	7·5	18·2	11·1	10·2	84·6
3	460	2·44	96·4	10·9	2·7	3·9	17·4	14·5	8·7	11·4	11·7	70·3
4	924	2·40	98·1	14·0	1·8	6·8	41·0	16·5	3·5	34·8	17·3	111·7
5	1,388	2·45	90·0	19·1	2·0	5·6	18·2	25·6	—	—	—	51·4
6	1,853	2·47	91·6	9·8	—	—	30·4	—	—	—	—	30·4
7	2,491	2·40	80·5	5·2	—	—	35·8	—	—	—	—	35·8
8	2,665	2·42	81·2	6·1	—	13·9	19·1	—	—	—	—	33·0

(1) Location: 30° 23·4′ N.; 119° 13′ W. Depth to bottom: 3,660 m.
(2) 40 l. of double-distilled water previously found to contain traces of fatty acids.
(3) Corrected to 100 per cent yield on the basis of the percentage recovery of the methyl esters.

Table 3. Organic Acids Isolated from Sea-Water by Co-precipitation with Ferric Hydroxide

Sample	Location	Depth collected (m.)	Depth to bottom (m.)	Volume extracted (l.)	Analysis (ash free)		Milligrams isolated		
					C	H	Total	Ash free	Per litre (ash free)
SFB—1	30° 49′ N. 119° 38′ W.	1,840	2,300	160	49·5	6·1	28·3	23·6	0·147
SFB—2	32° 45′ N. 121° 40′ W.	2,500	3,930	165	47·7	7·3	34·3	26·1	0·158
Control 1 (1)	—	—	—	—	—	—	2·0	—	< 0·011
Control 2 (2)	—	—	—	—	—	—	1·9	—	—

(1) Third re-precipitation of the original water from *SFB*—2 with ferric hydroxide and working up in the same manner as the original precipitates.
(2) Reagent control using distilled water and working up the ferric hydroxide precipitate as above.

extracts, freed of solvent, were plated on 1-in. copper planchets and counted with a Nuclear-Chicago model-*D*47 gas-flow counter. The free acids were then esterified and the methyl esters submitted to gas chromatographic analysis. The effluent methyl palmitate was collected from the column and counted to obtain the overall recovery. The yields and amounts of the saturated, mono-unsaturated and di-unsaturated acids based on the methyl palmitate recovery are shown in Table 2. There was no indication of the presence of the C_{15}, C_{17} and C_{19} esters in the tracer experiment.

The co-precipitation of organic acids with ferric hydroxide was effected by the initial addition of 10 mgm./l. of iron(III) as ferric chloride to each sample of filtered sea-water, previously acidified to a *p*H of 2–3 with hydrochloric acid. The ferric hydroxides sols were precipitated with 2 *N* potassium hydroxide to a final *p*H of 6·1–6·5, and the precipitate collected by centrifugation. This material was worked free of chloride ion, redissolved in hydrochloric acid to a *p*H of 2·0 and passed through 'Dowex-50' cation exchange resin (*H*-form, 200–400 mesh, 4× cross-linked). The acids were eluted with 0·1 *N* hydrochloric acid, and the eluate adjusted to a *p*H of 3·5 with 2 *N* potassium hydroxide. The solution was taken to dryness *in vacuo* and the residual salts extracted repeatedly with *iso*propyl alcohol. The alcoholic extracts, dried and freed of potassium chloride, were worked up to give light yellow solids, showing blue-green fluorescence, and giving negative tests for halogens, phosphorus, nitrogen, boron, sulphur and iron. The yields and carbon–hydrogen analyses of this material from two stations are shown in Table 3. The ash-free material gave an average molecular weight of 395 and an equivalent weight of 208. Hydroxyl and carboxyl groups were indicated by the infra-red spectra (Fig. 2) and spot tests. Tests for unsaturation and aromaticity were negative. Ultra-violet absorption curves showed only increasing absorption from 700 to 220 mμ. Attempts to separate this mixture by paper chromatography and paper electrophoresis were unsuccessful.

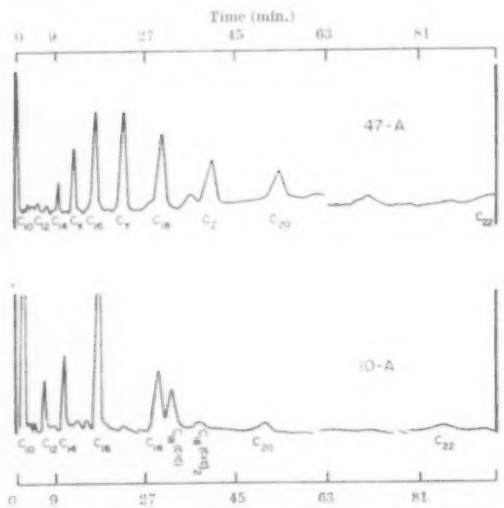

Fig. 1. Gas chromatographic traces of samples 47-A and 10-A

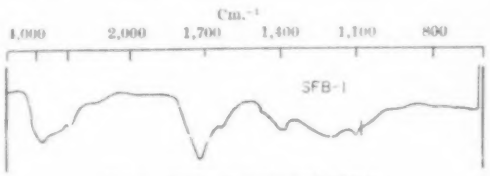

Fig. 2. Infra-red spectrum of *SFB*-1

A more detailed report and discussion of this work will appear elsewhere.

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Peter M. Williams*
Scripps Institute of Oceanography,
University of California,
La Jolla, California.

* Present address: Institute of Oceanography, University of British Columbia, Vancouver, B.C., Canada.

BIOPHYSICS

Use of Potassium Tartrate for Equilibrium Density-gradient Centrifugation of Animal Viruses

Density-gradient centrifugation of both the velocity and equilibrium types has been applied for separating and purifying plant viruses such as tobacco mosaic and potato yellows[1], and also very recently to animal viruses such as Rous sarcoma[2], Shope fibroma[3] and polyoma[4]. Equilibrium banding with satisfactory recovery of biological activity has usually been achieved in rubidium or caesium chlorides after centrifugation for approximately 24 hr. Some viruses are, however, inactivated by these salts, and others, as, for example, Rous sarcoma, require stabilization by albumin and citrate[2]. Non-equilibrium sedimentation in glycerol gradients has been used to purify Shope papilloma[3]; and reasonably sharp peaks of influenza and Newcastle disease viruses,

and also of vaccinia haemagglutinin, may be obtained after brief centrifugation in sucrose gradients of the velocity-sedimentation type[5].

In this communication we describe a simple method for equilibrium banding of some animal viruses, using preformed density gradients of neutral potassium tartrate. Equilibrium is obtained very rapidly in this salt, which possesses other advantages also in that concentrated solutions do not inactivate the infectivity or haemagglutinins of the various viruses so far examined. Furthermore, the salt is inexpensive and no additional purification of the analytical reagent is necessary.

Gradients were prepared at 4° using two small mixing chambers, one of which was filled with concentrated potassium tartrate (varying from 35 to 60 per cent in different experiments), and the other with 2 per cent tartrate. The *p*H of the solutions was adjusted to 7·5. Virus samples (0·25–0·5 ml.) were then graded on to the tartrate gradient in an equal volume of the 2 per cent salt. Centrifugation was carried out in the Spinco *SW*39 head at 39,000 r.p.m. Most viruses banded satisfactorily in equilibrium after 1–2 hr.; but vaccinia haemagglutinin, for example, may require 6 hr. centrifugation for close banding. After centrifugation, fractions were usually obtained by piercing the bottom of the centrifuge tube with a needle and running denser salt (70 per cent tartrate) up from below ('top unloader').

In some experiments the samples were collected by a novel method developed by one of us (R. S. E.), in which the centrifuge tube was lowered into a mixture of alcohol and dry ice and held there until the contents were frozen. The centrifuge tube was removed and cut rapidly into ten or more segments with a small saw. Each segment was then transferred to a tube and allowed to thaw. Contrary to expectation, control experiments showed that carefully controlled freezing did not distort or displace boundaries significantly, provided that the band was at least one-third of the way down the centrifugation tube. In several experiments, samples from equal volumes of virus centrifuged at the same time in the three buckets of the *SW*39 head were collected by three different methods, namely, dripping from the bottom of the tube, dripping from the top of the tube in the top-unloader, and by 'freezing-and-sawing'. In every instance the latter technique yielded as sharp, and frequently sharper, bands than those obtained by dripping. The freezing-and-sawing technique also offers the advantage that each fraction is collected independently, and there is thus less danger of contamination from one fraction to another than when all the samples are passed through the same orifice.

A typical sedimentation diagram from a sample of influenza *A* virus centrifuged in a tartrate gradient is shown in Fig. 1. It will be seen that after centrifugation for only 40 min. the majority of haemagglutinin is recovered in equilibrium in a single fraction, and that only traces of activity are recovered in adjacent tubes of higher or lower densities. Equally sharp equilibrium peaks were obtained with influenza *B* and Newcastle disease viruses. In all cases the recovery of haemagglutinin and infectivity was quantitative; and with Newcastle disease virus the titre of the most active haemagglutinin fraction was actually from two- to four-fold higher than that of the original virus. The latter effect is presumably due to the removal of an inhibitor elsewhere on the

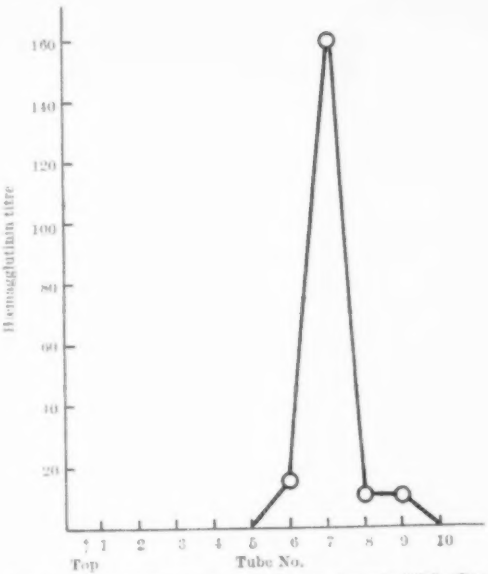

Fig. 1. Sedimentation diagram of influenza *A*, strain *MEL*, after centrifugation in a potassium tartrate gradient for 40 min. at 39,000 r.p.m. in the Spinco *SW*39 head. Maximum potassium tartrate concentration, 43 per cent. Virus diluted 1 : 2 in buffered normal saline, and 0·25 ml. placed on gradient

gradient. The specificity of each haemagglutinin was checked by neutralization with the appropriate antiserum. The most concentrated tartrate solution used (60 per cent) agglutinates a 1 per cent suspension of chicken erythrocytes to a dilution of 1 : 2–1 : 4 only.

Potassium tartrate gradients are thus more convenient in many ways than gradients prepared with heavy salts such as cæsium and rubidium chlorides for equilibrium banding of several animal viruses. It seems likely that tartrate gradients could readily be applied for the concentration and purification of many other viruses and macromolecules, for the separation of virus mixtures, and for the separation of components from one virus. For example, as will be described in detail elsewhere, the vaccinia haemagglutinin may be banded relatively sharply in 45 per cent potassium tartrate, whereas most of the infectious particles are found at the bottom of the gradient at this concentration[6]. Experiments are in progress in an attempt to sharpen the resolution of these and other viral components.

We are indebted to Dr. Carl Woese for valuable advice on gradient techniques. This work was supported by a research grant (*E* 2213-*C*2) of the U.S. Public Health Service, and by a grant from the Committee on Atypical Growth, Yale University.

J. F. McCrea
Richard S. Epstein
William H. Barry

Department of Biophysics,
Yale University,
New Haven, Connecticut.

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CHEMISTRY

Rapid Identification of High Polymers using a Simple Pyrolysis Unit with a Gas–Liquid Chromatograph

For some years it was standard practice in these laboratories to pyrolyse polymers in an intimate mix with ignited silver sand under carefully controlled conditions in an inert partial atmosphere. The degradation products were fractionated and examined by gas–liquid partition chromatography. The performance of the entire process in one stage was considered as a natural development of the technique, and the piece of apparatus to be described is now in regular use.

The considerations of design and operation of the pyrolyser were governed by the following factors: (*a*) The polymer degradation must be complete and should occur in the shortest possible time. A very thin film of polymer is therefore required and this will have the great advantage of minimizing secondary reactions between degradation products[1]. (*b*) 'Flash' depolymerization requires rapid heating of the very thin polymer film to the degradation temperature. This may be achieved by a large heating area relative to the mass of polymer. (*c*) Gaseous diffusion of the degradation products must be a minimum, therefore the pyrolysis coil must be in the chromatographic column itself and sited as near the surface of the packing material as is practicable. (*d*) To reduce the risk of condensation of any part of the gaseous sample the pyrolysis coil must be located within the column heater zone.

The pyrolyser (Fig. 1) consists of a rubber bung through which pass two pieces of 6 *BA* brass studding about 4·25 in. long; they project 1·5 in. above the bung and 2 in. below it. The upper ends are sleeved with polyvinyl chloride and terminate in a 5-amp. connector block, the lower ends are glass sleeved and terminate in screwed connector bushes. The pyrolysis coil itself is a 6-in. length of 28 standard wire gauge nichrome wire coiled to 4-mm. diameter over its middle 4 in., the two ends being fixed in the two screwed connector bushes. The associated electrical circuit is shown in Fig. 2.

Fig. 1. Two views of the pyrolyser in position in a modified chromatographic column (quarter actual size)

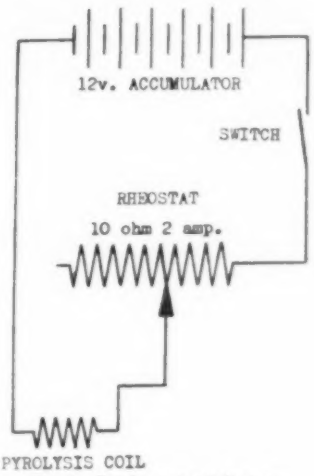

Fig. 2. Pyrolyser circuit diagram

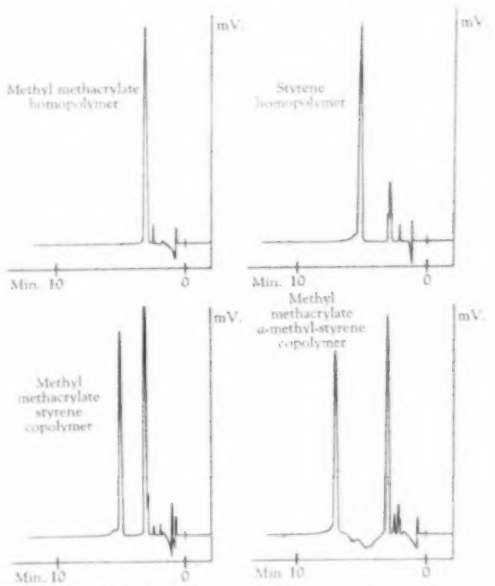

Fig. 3. Pyrolysis chromatograms of two homopolymers and two copolymers obtained on a 12·5 per cent polyethylene glycol succinate column operating at 80° C.

A very thin film of polymer, from a dilute emulsion or solution, or a dispersed gel, is cast on the filament, dried, and the assembly inserted in the top of a modified chromatographic column. The carrier gas flow is then started, and, after allowing a short time for the flow equilibrium to be set up, the coil is 'fired' at about 500° C. for 2–5 sec. The pyrolysis products are immediately swept on to the column by the carrier stream and chromatographed. Completeness of degradation can be checked by re-firing the coil at 1,000° C. when there should be no further signal from the detector due to degradation products.

Characteristic fingerprint chromatograms for homopolymers of methyl methacrylate and styrene, and copolymers of methyl methacrylate with styrene and methyl methacrylate with α-methyl-styrene, are shown in Fig. 3. When examining copolymers such as these, reliable quantitative assays of the monomers can be obtained, but with more complex monomers and co-monomers the method is only semi-quantitative.

Future modifications will include a precise method of filament temperature measurement, a filament of lower heat capacity—possibly in the form of a strip—and the development of a miniature version of the apparatus.

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C. E. Roland Jones
A. F. Moyles

Research Department,
Vinyl Products, Ltd.,
Carshalton, Surrey.

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An Enrichment Trap for Use with Capillary Columns

In the course of an investigation into the volatile substances produced during the cooking of potatoes, difficulties were experienced when using gas chromatographic techniques[1] in the injection of small quantities of vapour. A nylon capillary column, length 50 ft., internal diameter 0·01 in., coated with 15 per cent tritolyl phosphate, and a Lovelock small detector[2] were used. It was found that the conventional injection by syringe into a 100 : 1 by-pass system did not allow sufficient vapour to pass into the column. The by-pass of argon carrier gas could be reduced to 30 : 1 without seriously impairing the resolution of the components being studied, but this still did not provide sufficient sample for detection. This method of injection was abandoned in favour of an enrichment trap. The enrichment trap technique for use with packed columns has been described[3].

The volatile substances given off from 1 kgm. of potatoes boiling in a 3-litre round-bottom flask were removed by a stream of nitrogen and freed from water vapour by passing successively through a glass U-shaped trap, cooled with solid carbon dioxide—acetone, and a similar trap cooled with liquid oxygen. The escaping volatile substances were then retained in a U-shaped trap consisting of 10 in. of 0·01 in. diameter nylon capillary coated with the same phase as the column. After collection for 20 min., the trap was disconnected and re-connected to the nylon capillary column (Fig. 1), while still immersed in liquid oxygen. With the carrier gas flowing, the trap was kept at − 183° C. until the air peak signal was obtained on the recorder, and then immersed in hot water at approximately 60° C. for 20 sec., removed, and left at room temperature. The chromatogram obtained showed a good separation of components, along with a small air peak which was a useful guide for obtaining relative retention times.

Confirmatory infra-red analysis cannot be obtained when using the nylon capillary column. The enrichment trap can, however, be used satisfactorily for mixed chromatography. The capillary trap is filled

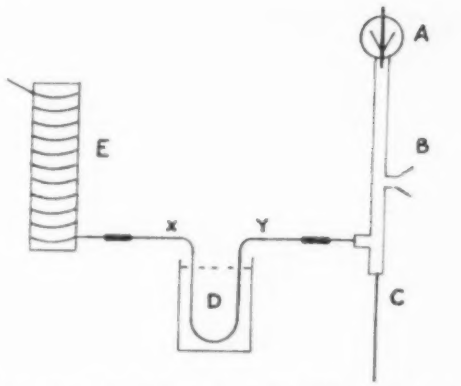

Fig. 1. *A*, Argon flow regulator; *B*, syringe injection port; *C*, nylon capillary by-pass; *D*, enrichment trap immersed in liquid oxygen; *E*, 50-ft. nylon capillary column. Volatile substances are collected in the trap with the gas flowing in an *XY* direction, but released as shown (ref. 3)

with unknown volatile substances as described above, then connected to the column as before and a small sample of authentic vapour, suspected to be present in the unknown, injected by syringe into the port situated in front of the 30 : 1 by-pass system. Thus 1/30th of the sample passes into the trap and is retained. The capillary trap is then disconnected from the column system and connected to a similar empty trap held in liquid oxygen. The original trap containing the unknown volatile substance and authentic sample is immersed in hot water causing the contents to mix intimately. A hyperdermic syringe needle is fitted to the first trap and an open syringe is used to propel the volatile substances from the first trap to the second trap. The second trap is then connected to the column as before and the contents chromatographed. The two-trap system is necessary since it was found that intimate mixing did not occur in the first capillary trap.

I wish to acknowledge the encouragement given by Mr. A. E. Joyce.

R. Self

Research Establishment,
Ministry of Agriculture, Fisheries and Food,
Aberdeen.

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Thermal Stability of Titanium Dioxide

Vorres and Dutton[1] and Vorres and Donohue[2] have recently described the preparation and crystal structure of titanium dioxide. Its decomposition in dry and moist air and dry nitrogen has been determined as part of our investigations of the thermal decomposition of some inorganic fluorides.

The results presented in Table 1 were obtained by the use of an atmosphere-controlled thermogravimetric balance the construction and operation of which have been described elsewhere[3]. The reported isothermal weight-loss data for runs 3 and 4, made in dry air and nitrogen, are maximum losses, and the X-ray examinations of their residues showed only titanium dioxide (anatase). Several additional experiments were carried out in a horizontal 'Vycor'

Table 1. Isothermal Weight-loss Data for Titanium Dioxide

Run No.	Temperature (deg. C.)	Atmosphere	Duration of the run (min.)	Total weight-loss (per cent)
1	340	dry air	4,285	47·0
2	400	dry air	1,350	54·9
3	460	dry air	112	60·0
4	440	dry nitrogen	393	59·9
5	340	moist air	330	22·3
6	400	moist air	186	24·2
7	455	moist air	88	28·5

tube at 460° C. with a stream of dry air flowing through the tube. In these experiments a white material condensed on a water-cooled cold finger placed 2 in. from the heated sample contained in a platinum boat. This condensate was very hygroscopic and reacted vigorously with water to form a clear, colourless, highly acidic solution which gave positive qualitative tests for both titanium and fluoride ions. These results agree well with the reported characteristics[4,5] of titanium fluoride. It was concluded that the fluoride formed during the decomposition of titanium dioxide and was swept away by the air stream (b.p. of titanium fluoride is 284° C.[5]).

From this information it was concluded that titanium dioxide in a dry atmosphere of air or nitrogen decomposed as follows:

$$2TiOF_2 = TiO_2 + TiF_4 \quad (1)$$

The calculated loss of weight on the basis of this equation, if all the fluoride is lost, is 60·8 per cent, which is in good agreement with runs 3 and 4. Fig. 1 indicates that this decomposition begins at 150–200° C. and is complete by 500° C. when the heating-rate is 4° C. per min.

The weight-loss values for runs 5, 6 and 7 made in a moist atmosphere are maximum values. X-ray patterns of the residues show only titanium dioxide (anatase). From this evidence the simplest reaction is written as:

$$TiOF_2 + H_2O = TiO_2 + 2HF \quad (2)$$

If only hydrogen fluoride is lost, the calculated loss of weight is 21·6 per cent. This value agrees well with run 5. However, the observed losses of runs 6 and 7 are noticeably greater.

The following explanation for the observed deviations of runs 6 and 7 is suggested. Reaction (2) can be considered as the summation of the two reactions:

$$2TiOF_2 = TiO_2 + TiF_4 \quad (3)$$

$$TiF_4 + 2H_2O = TiO_2 + 4HF \quad (4)$$

If reaction (3) is the first step, then the loss of any titanium fluoride from the crucible before it is hydrolysed to titanium dioxide will cause a loss of weight in excess of that calculated for reaction (2).

It will be noted that the deviation from the expected loss on the basis of the simple one-step case (reaction (2)) increases for higher-temperature runs. At higher temperatures it was observed that the velocity of the decomposition was greater, so the probability of escape of titanium fluoride before it can react with water vapour in the atmosphere is also greater. This effect also depends, among other things, on the partial pressure of the water in the atmosphere, which was not considered.

A similar deviation with respect to increasing temperature was observed in the decomposition of Na_2SiF_6 in moist air[3].

J. S. Machin
D. L. Deadmore

Illinois State Geological Survey,
Urbana,
Illinois.

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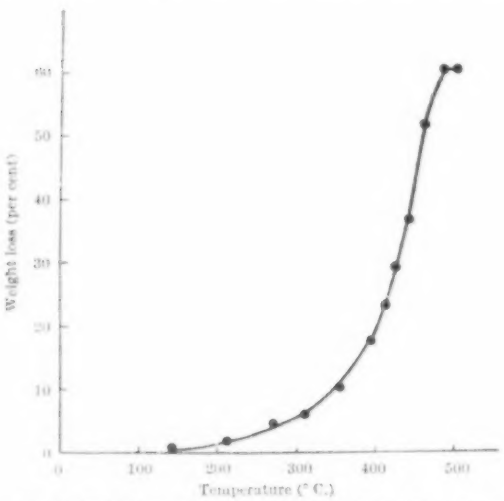

Fig. 1. Weight-loss of titanium dioxide heated at the rate of 4 deg. C. per min. in dry air

Ethyl Branching in the Fischer–Tropsch Synthesis

Current schemes for explaining chain-growth in the Fischer–Tropsch synthesis[1–3] do not permit the formation of an ethyl-branched hydrocarbon. We wish to report the identification of 3-ethylpentane in a hydrogenated Fischer–Tropsch synthesis product. A compound with this carbon skeleton has not hitherto been found in the product. Quantitative analyses by gas chromatography give a mole ratio of 2,3-dimethylpentane to 3-ethylpentane of 1·5. Weitkamp[1] found that 2,3-dimethylpentane constituted 0·9 volume per cent of the hydrogenated C_7-hydrocarbons from the synthesis product.

The Fischer–Tropsch product was made by passing 1 hydrogen : 1 carbon monoxide gas over a reduced-iron catalyst at 260° C., 21·4 atmospheres, and an hourly space-velocity of 300. The product was distilled to give four fractions, boiling from 60° to 170° C. These fractions were hydrogenated over platinum oxide catalyst. (It has been shown[4] that the distribution of skeletal isomers in the Fischer–Tropsch synthesis is identical for paraffins and olefins.) These hydrogenated fractions were chromatographed on Davison No. 950 silica gel, at column temperatures from − 10° to + 5° C., to isolate the hydrocarbon portions. Olefin-containing portions were re-hydrogenated and re-chromatographed. The combined saturated-hydrocarbon fractions were then distilled into narrow-boiling fractions.

Gas-chromatographic examination of these hydrocarbon fractions was made on a 26·5 ft. by 4·5 mm. internal diameter stainless steel column, coiled as a helix, containing 79 gm. of packing made in the weight ratio 12 parts tri-cresylphosphate to 88 parts 35–45 mesh 'Chromosorb'. By measuring the retention time relative to 2-methylhexane, a compound known to be present, 3-ethylpentane, was identified in these fractions.

Confirmation of 3-ethylpentane in these fractions was obtained by trapping-out the gas-chromatography peak at liquid nitrogen temperatures and analysing the 'freeze-outs' on a mass spectrometer. The 3-ethylpentane peak and part of the immediately preceding 3-methylhexane peak were in the freeze-outs. The hydrocarbon portions of duplicate freeze-outs analysed as 87 per cent 3-ethylpentane, 13 per cent 3-methylhexane, and 88 per cent 3-ethyl pentane, 12 per cent 3-methylhexane.

In the Fischer–Tropsch synthesis, 3-ethylpentane might be formed in any one of several ways: (1) The carbon chain might grow by adding a one-carbon unit to a methyl branch already present such as in the 3-methylpentane chain. (2) A one-carbon unit is added to 2-ethyl-1-butene (Weitkamp[1] shows that this is present in the product) by an oxo-type reaction. (3) Reaction occurs between a C_2-chain and a two-carbon unit, that is, 'multiple build-in' as suggested by Hall *et al.*[5]. (4) Isomerization of the carbon skeleton occurs to form 3-ethylpentane, but this seems unlikely.

This work is part of a larger project on the analysis of Fischer–Tropsch synthesis products through the C_7-compounds. The work in its entirety will be reported later. We wish to acknowledge the following who have contributed to this particular phase of the work: C. Zahn, G. Pantazoplos and A. G. Sharkey, jun.

Bernard D. Blaustein
Irving Wender
Robert B. Anderson

Bureau of Mines,
U.S. Department of the Interior,
Pittsburgh 13,
Pennsylvania.

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BIOCHEMISTRY

Hæmoglobins, Myoglobins and Erythrocruorins: a Proposal for modifying the Present Terminology

The present terminology for those protohæm respiratory pigments which combine reversibly with oxygen, in which the terms hæmoglobin, myoglobin and erythrocruorin are used in varying senses by different authors, is far from satisfactory. Keilin and Hartree[1] showed that a convention introduced earlier by Svedberg[2], whereby all invertebrate pigments of this type were to be designated as erythrocruorins, was no longer justified on the basis of current knowledge. They suggested instead that 'hæmoglobin' should be used as a general term for both vertebrate and invertebrate pigments, and that the term erythrocruorin should be abandoned. According to their suggestion any given pigment should be identified by its origin, as in *Planorbis* hæmoglobin, muscle hæmoglobin, etc. It is with regard to the latter designation that this terminology immediately ran into difficulties.

I may recall that at the time when Keilin and Hartree made their proposal it was generally held that myoglobin (muscle hæmoglobin) and hæmoglobin in vertebrates were fundamentally different, and differences between them were always emphasized. Thus, Roughton, quite recently, commented[3] that: "It is an old creed that these two compounds are physicochemically similar, but this creed must now go, for the more intimately one studies them, the more frequent are the differences that one finds". Hence, Keilin and Hartree's proposal to equate myoglobins with hæmoglobins did not meet with general acceptance. However, following the work of Kendrew *et al.*[4,5], and of Perutz *et al.*[6], it might appear that such a proposal could now be defended. Yet the net result of the X-ray work, which proves that the tertiary structure of mammalian myoglobin and hæmoglobin is very closely similar, has been to demonstrate that there are at present no physicochemical criteria by which one can distinguish between these compounds in all cases. It might seem, therefore, that we should abandon the term myoglobin, and use instead the older names, muscle hæmoglobin or tissue hæmoglobin. Yet this is not so since there is a very real distinction to be made between the two, which is implicit in the term "tissue hæmoglobin". Hæmoglobins function in the transport of oxygen to the tissues and therefore occur in conjunction with some kind of circulatory system. They may or may not be found in corpuscles. Myoglobins are usually saturated with oxygen, remain within the tissues where they are located, and function to provide a reserve of oxygen against short-term deficits.

Keilin and Hartree summed up their intentions thus: "To avoid confusion and unnecessary complications of the nomenclature, the classification of all biologically active protein compounds, such as oxygen carriers or enzymes, should be based not upon their physico-chemical properties as proteins but upon their specific biological activities and the nature of their active, or prosthetic, groups". The distinction between myoglobins and hæmoglobins, made above, is in line with this aim. However, it is obviously unsatisfactory to use 'hæmoglobin' as a generic name for both groups of pigment. Furthermore, it would have the very real disadvantage that for many investigators 'hæmoglobin' means a compound with four hæm groups per molecule, with molecular weight 68,000, and all the other properties of mammalian hæmoglobins. Finally, one requires a term which carries no connotations of any sort other than that the pigment contains protohæm and combines reversibly with oxygen, for use in those cases where the given pigment cannot be classed as either myoglobin or hæmoglobin through lack of data; and possibly also if it should be found impossible to do so. For example, the recent work of Scholander[7] has raised the possibility, which seems especially attractive when considering certain invertebrate animals, that tissue pigments may act to promote

the passage of oxygen to the tissues, rather than, or in addition to, carrying a reserve of oxygen. (The storage hypothesis has not found favour with investigators in certain specific cases, compare Eliassen[8].)

It is now possible to conceive a classification which takes account of these considerations, which has historical and logical justification, and which causes the least change to the existing terminology. The term 'erythrocruorin' (red pigment) was introduced by Lankester[9] as a general term for all protohæm oxygen-combining respiratory pigments, without any implication as to the structure or function of the pigment, and in contrast to the analogous pigments of certain marine worms which he called 'chlorocruorins' (green pigment)—a term which is still used in this sense[10]. It is therefore proposed that the term erythrocruorin be used for all known or presumed protohæm respiratory pigments which are known or presumed to be capable of undergoing reversible oxygenation. All erythrocruorins which are known or presumed to function in oxygen storage can be classed as myoglobins. It will be noted that this scheme maintains the present usage for vertebrate erythrocruorins, but also incorporates it into a general scheme for both vertebrate and invertebrate pigments.

It may be noted also that the prefix 'myo-' could possibly be used for pigments other than erythrocruorins which are analogous to myoglobins. Manwell[11] has already used the term myohæmerythrin in this sense.

Consistent use of the terminology suggested here will be found to lead not only to greater flexibility in discussion but greater precision also. It is hoped that these advantages, together with those enumerated above, will commend themselves to other workers in the field.

Malcolm H. Smith

John Harrison Laboratory of Chemistry,
University of Pennsylvania,
Philadelphia 4.

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Rehardening of Softened Enamel Surfaces of Human Teeth by Solutions of Calcium Phosphates

Rehardening of softened human enamel has been attempted in the past[1-3], but has not been clearly demonstrated since the earlier workers were not able to show that the softened material was not lost. Knoop hardness measurements provide a quantitative and sensitive measure of surface changes, and any loss of surface can be shown by alterations of the size and shape of the previously placed indentations. This communication describes conditions which have been developed for rehardening tooth surfaces, softened by a prior treatment with a buffer.

A Kentron microhardness tester was used with Knoop diamond indenter, as described previously[4,5], for following changes in surface hardness. Human teeth were tested for hardness initially, after softening by acetate buffer, and after treatment in calcium phosphate solutions. For each determination, ten indentations were made, and the hardness was expressed as an average Knoop hardness number. The initial indentations were often remeasured at the end of the experiments, and no change of length was noted. Softening of the teeth was produced in groups of ten by treatment with 1 litre of acetate buffer 0·001 *M*, *p*H 5·50, for 2–12 hr. at 37°.

For the preparation of rehardening solutions, two calcium salts were used, secondary calcium phosphate dihydrate (calcium/phosphorus molar ratio, 1·0) and synthetic hydroxyapatite (Ca/P ratio, 1·67). A weighed amount of salt (50 m.moles of calcium) was dissolved in twice this molar concentration of hydrochloric acid, and the volume was made up to 1 litre. From this stock solution, aliquots corresponding to 0·75 or 1·25 m.moles of calcium were pipetted into bottles containing distilled water at 37°. Aliquots of potassium fluoride stock solution (0·02 *M*) corresponding to 1–7 p.p.m. were added, if desired. The volume was made up to about 480 ml. with distilled water and sufficient potassium hydroxide (0·05 *M*) was added to bring the *p*H to predetermined values. The final volume was adjusted to 500 ml. The solutions were metastable, the *p*H dropped during the period of treatment, and some precipitation occurred.

Softened teeth were kept in pairs in 500 ml. of the rehardening solutions at 37° C. without stirring, and their hardness was determined at various time-

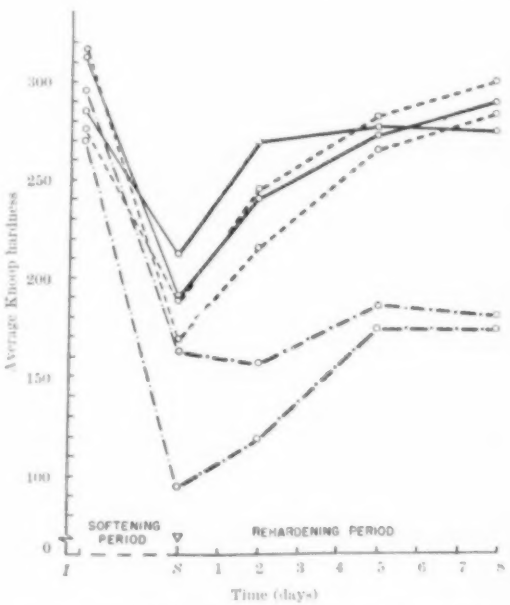

Fig. 1. Rate of rehardening of softened enamel surfaces as related to the extent of softening. *I*, Initial hardness; *S*, hardness after treatment with acetate buffer for 2 hr.; ——: 4 hr., – – –; 8 hr., — · — · —. Rehardening solution: Ca, 2·5 m.moles/l.; Ca/P, 1·0; *p*H 7·0; changed every 24 hr.

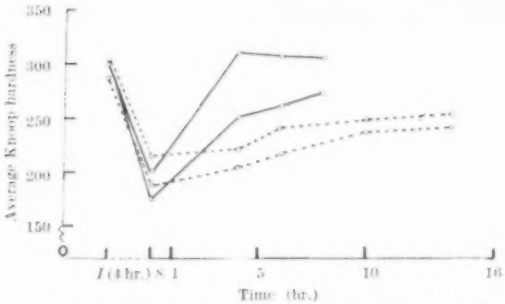

Fig. 2. Effect of fluoride on the rate of rehardening of softened enamel surfaces. *I*, Initial hardness; *S*, hardness after softening in acetate buffer for 4 hr. 1 p.p.m. fluoride, ——; no fluoride, – – –. Basic rehardening solution: Ca, 1·5 m.moles/l.; Ca/P, 1·67; *p*H 7·3; changed every 2 hr.

intervals as indicated in Figs. 1 and 2. The results in this communication are representative of rehardening experiments involving a total of more than 300 teeth.

Fig. 1 gives the results for individual teeth obtained with solutions prepared from the secondary calcium salt (Ca/P ratio, 1·0) and changed daily. Preliminary results of this type were reported earlier[6]. Four of six teeth showed a return to the initial hardness after treatment for 8 days. The two teeth that did not show considerable rehardening were those softened for 8 hr. to a low hardness. This and other similar results showed that complete rehardening did not occur if the softening process had proceeded too far, below about 150 Knoop hardness number. This limit may be of considerable interest in that it may be the boundary between sound and carious enamel and represent the limit of possible natural reparative recalcification of enamel. Sobel and his associates[7] have shown that calcification takes place in two discrete stages, nuclei formation and subsequent crystal growth. The remineralization of these experiments may refer only to the stage of crystal growth.

The rate of rehardening was found to be more rapid for solutions with Ca/P ratios of 1·67, especially in the presence of small amounts of fluoride. The results are shown in Fig. 2. The teeth kept in 500 ml. of solution containing 1 p.p.m. of fluoride regained the initial hardness in 4 hr., whereas in the absence of fluoride the recovery was much slower.

The accelerating effect of fluoride ions on the rehardening of enamel adds a second explanation for the mechanism of fluoride protection from dental caries. In addition to producing more insoluble enamel, fluoride ions appear to affect the dynamic equilibrium between tooth surfaces and the oral fluid by accelerating the enamel remineralization.

Table 1. Inhibition of *in vitro* Caries in the Artificial Mouth in the Presence of Rehardening Solutions
(Calcium/phosphate, 1·67; calcium, 1·5 m.moles/l. fluoride, 0·3 m.moles/l., *p*H 7·1. Freshly prepared medium was used twice daily)

Hardness (Knoop hardness number)*			
Experimental (Culture medium + rehardening solution)		Control (Culture medium alone)	
Initial	After 5 days	Initial	After 5 days
188	176	235	86
226	205	282	81
262	269	261	96
278	262	249	82
295	283	273	29
248	285	291	29

* Average *S.D.* ± 14

The rehardened enamel was tested for resistance to abrasion by tooth brushing and for resistance to softening by a second exposure to the acetate buffer (*p*H 5·50) for 2–4 hr. Brushing caused no appreciable loss of surface material. For 34 teeth, the average rate of softening by the buffer was 19 ± 3 Knoop hardness number/hr. for the rehardened teeth as compared with 26 ± 6 Knoop hardness number/hr. for the original surfaces.

In the artificial mouth[8], teeth exposed to oral bacteria and a culture medium supersaturated with calcium phosphate and containing 6 p.p.m. fluoride were essentially unaltered after 5 days exposure (Table 1). The controls were softened to the limit of the sensitivity of the measurements.

This evidence for enamel rehardening emphasizes the dynamic nature of the enamel surface and the importance of the oral fluid in the carious process. Prevention and healing of initial carious lesions seem possible by modification of the composition of the oral fluid either systemically or locally.

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Theodore Koulourides
Heriberto Cueto
Ward Pigman

Department of Biochemistry,
University of Alabama,
Medical Center,
Birmingham,
Alabama.

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Biliverdin in the Eyes of *Polyphemus pediculus* (L.) (Crustacea, Cladocera)

The large median compound eye of the Cladocera begins its development as two separate rudiments which enlarge gradually and fuse in the mid-line. In the majority of Cladocera these rudiments are red in colour and gradually darken so that they are black just before fusion. In embryos of *Polyphemus pediculus* the eye rudiments are green in colour, and when treated with yellow nitric acid they give a positive Gmelin reaction, indicating the presence of a bile pigment.

A large sample of female *Polyphemus*, containing numerous embryos, was first extracted with acetone to remove carotenoids and then extracted with acid methanol (5 per cent hydrochloric acid), giving a deep olive-green solution. When this was diluted with water and shaken with chloroform the chloroform phase became blue in colour while the acid methanol phase became orange-brown. The chloro-

form phase was washed with dilute sodium bicarbonate, then with water and evaporated to dryness. When the pigment was redissolved in acid methanol the absorption spectrum showed a sharp peak at 374 mμ and a lower, more rounded, peak at 685 mμ. These are close to the absorption maxima of biliverdin hydrochloride; the small differences can be attributed to the presence of other substances in the extract.

The identity of the green pigment as biliverdin was confirmed by the addition of zinc acetate and a little iodine to a methanol solution in the presence of a trace of ammonia. The result was a green solution with a brilliant pink fluorescence in ultra-violet light, and a sharp absorption band at 635 mμ showing that the pigment had proto not meso side-chains.

The presence of biliverdin in the eyes of adults was demonstrated by selecting females without embryos and extracting with methanol. The addition of zinc acetate and iodine produced the same results as with the larger sample.

It has not been possible to demonstrate a Gmelin reaction in the eyes of adult *Polyphemus* because of the presence of large amounts of a dark masking pigment. This pigment is also extracted with acid methanol, but remains in the methanol phase when it is diluted and shaken with chloroform. Further studies are being made of this and similar pigments in other Cladocera; meanwhile, it is possible to say that they are similar in many respects to ommochromes, being insoluble in most organic solvents, but easily soluble in acids, and showing reversible changes in colour according to whether they are oxidized or reduced.

Biliverdin is rare in the Crustacea; it has been found only in the digestive gland of the crayfish *Cambarus*[1], and in the roots of certain parasitic cirripedes[2]. The present record of biliverdin in *Polyphemus* adds another crustacean order to the few known to include bile pigments in their metabolism[3]. It is interesting in this connexion to note that, although searched for, no bile pigments have been found in the cladoceran *Daphnia*[4].

J. Green

Zoology Department, Bedford College, Regent's Park, London, N.W.1.

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PHYSIOLOGY

Magnesium Absorption in Sheep

Low levels of dietary magnesium precipitate hypomagnesæmia experimentally in lambs[1]. It is not known whether these findings are related to the hypomagnesæmia which occurs spontaneously in adult ruminants near parturition in autumn and spring on some pastures. The present communication reports an attempt to produce hypomagnesæmia in sheep, but with a different type of roughage-containing diet.

Lambs born the previous year were fed the experimental rations beginning in June. Sheep 1 (Border × Clun cross) had previously been on a high plane of nutrition, that is, good pasture; sheep 2 (Border × Suffolk cross) had been on a low plane of nutrition, that is, stubble. A diet relatively low in magnesium was fed (Table 1) and distilled water supplied for

Table 1
Chemical analysis (dry-weight basis)

Feeding stuff	Magnesium (per cent)	Calcium (per cent)	Phosphorus (per cent)
Fodder cellulose	0·16	0·825	0·063
Molasses	0·28	0·94	trace
Flaked maize	0·109	—	0·195
Lucerne hay	0·233	1·97	0·288
$Ca_3(PO_4)_2$	—	38·7	20·2
NaCl	—	—	—

Mineral composition of daily ration during test period (dry weight basis)

Sheep 1. (Final live weight = 96 lb.)

Feeding stuff	Amount fed (gm.)	Total magnesium (gm.)	Total calcium (gm.)	Total phosphorus (gm.)
Fodder cellulose	460	0·736	3·80	0·29
Molasses	23	0·065	2·15	—
Flaked maize	174	0·190	—	0·34
Lucerne hay	428	0·997	8·44	1·23
$Ca_3(PO_4)_2$	9	—	3·48	1·82
NaCl	9	—	—	—
Total per day		1·988	17·87	3·68

Sheep 2. (Final live weight = 66 lb.)

Feeding stuff	Amount fed (gm.)	Total magnesium (gm.)	Total calcium (gm.)	Total phosphorus (gm.)
Fodder cellulose	276	0·442	2·28	0·174
Molasses	23	0·065	2·19	—
Flaked maize	87	0·095	—	0·170
Lucerne hay	342	0·798	6·75	0·987
$Ca_3(PO_4)_2$	9	—	3·48	1·820
NaCl	9	—	—	—
Total per day		1·400	14·70	3·151
During urea feeding (+ 184 gm. cellulose)		(1·72)	(16·22)	(3·097)

consumption *ad libitum*. The calcium intake was kept at a high level, since an inter-relationship between calcium and magnesium availability is well substantiated. The magnesium content of the diet was higher than had been hoped probably due to the inclusion of mineral salts from tap-water used to wash the fodder cellulose prior to the drying process.

The overall percentage of magnesium in the ration was about 0·18 per cent (dry weight basis) compared with 0·02 per cent (air-dry basis) used by other workers[1] and hypomagnesæmia was not observed in the sheep (Table 2). Feeding stuffs were analysed, after ashing, for calcium[2] and magnesium[3]; total phosphorus determinations on feeding stuffs followed wet oxidation with sulphuric acid/hydrogen peroxide[2]. The same methods were applied directly to blood serum.

Table 2. Blood Serum Magnesium, Calcium and Inorganic Phosphorus (mgm./100 ml. serum)

	Magnesium				Calcium				Inorganic phosphorus			
	A	*B*	*C*	*D*	*A*	*B*	*C*	*D*	*A*	*B*	*C*	*D*
Sheep 1	1·9	2·5	2·1	2·2	11·6	11·0	10·8	10·7	5·6	5·3	4·9	6·1
Sheep 2	2·0	2·3	1·9	2·0	9·9	9·2	9·5	8·9	7·4	7·1	6·2	8·2

A, Basal sample; *B*, low-magnesium ration for 19 days; *C*, low-magnesium ration for 36 days; *D*, low-starch low-magnesium ration with urea for a further 29 days.

A comparison of the diets used in different experiments is of interest. Recently it has been suggested that dietary phytate may inhibit magnesium absorption from the intestine of the rat[4]. The use of corn cobs by McAleese and Forbes in the diet of the lambs and in the bedding[1] would imply a high intake of phytate compared with the small amounts of phytate provided by flaked maize and lucerne hay in the diet listed in Table 1. The competition of phytate for magnesium may exacerbate the already low-magnesium intake, as in the experiments of McAleese and Forbes[1], and so account for the very rapid onset of hypomagnesæmia. Hence the possibility that

dietary phytate is a factor in spontaneous hypomagnesæmia needs to be examined, as this competitive effect may occur in the ruminant as well as in the monogastric animal.

A further known factor concerned with magnesium absorption in cows is the level of rumen ammonia[5]. Introduction of large amounts of ammonium acetate and carbonate into the rumen via a fistula reduced both the urinary magnesium excretion and the serum magnesium-levels. Feeding 10 gm. of urea daily, which presumably forms ammonia *in vivo*, did not lead to hypomagnesæmia in sheep on a reduced magnesium intake (Table 2). The rise in serum inorganic phosphorus-level after urea feeding is unexplained; release of phosphate previously bound to phytate would certainly increase the effective phosphorus intake. Flaked maize was omitted from the diet during urea feeding since low-starch rations favour urea toxicity and presumably ammonia production[6].

Only an approximate comparison of the relative amounts of ammonia supplied can be made. Ammonium acetate or carbonate was administered to cows via rumen fistulæ at a rate of about 20–30 gm. ammonia per 100 lb. body-weight[5] compared with about 6·9 gm. ammonia per 100 lb. body-weight given as urea to the sheep.

This evidence reinforces current theories that spontaneous hypomagnesæmia is more complex than a simple nutritional deficiency. Environmental, genetic and endocrine factors may also be concerned in the aetiology of this aberration.

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D. F. Evered*

School of Agriculture,
University of Cambridge.

* Permanent address: Chemistry Department, Chelsea College of Science and Technology, London, S.W.3.

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Bioassay of Ciguatera Toxin

The tropical fish poisoning known as 'ciguatera', which is clearly different from the well-documented tetraodon poisoning, has long been known in the Pacific. Its narrow regional appearance and its variability within a given species of marine fish have been puzzling phenomena. The symptoms associated with ciguatera have been well described, but fundamental knowledge of the toxin is virtually non-existent. The present state of this problem has recently been reviewed by Randall[1].

As the first stage of an investigation aimed at the isolation and identification of the toxic principle, it was necessary to develop a reliable bioassay. The bioassay which had been devised for *Gonyaulax* toxin from shellfish[2] was used and standardized for ciguatera toxin[3] by Halstead and Bunker[3]. A re-investigation of this method in this Laboratory proved that this assay could not be employed with confidence and emphasized the necessity of finding an unambiguous bioassay. As is shown by the results in Table 1 aqueous extraction of toxic fish as described by Halstead and Bunker[3] failed to extract the toxin. It was found that fish or fish extract could be screened for toxicity by feeding raw fish or extract residue mixed with egg to the mongoose (*Herpestes mungo*). This animal exhibits symptoms not unlike those which have been described for humans following ciguatera poisoning. With this qualitative assay it could be shown that ethanol will extract efficiently the toxin from *Lutjanus bohar* (Forksål) collected in the Line Islands and known to be toxic as a result of mongoose feeding. The extraction residue after removal of the ethanol *in vacuo* was injected intraperitoneally into mice. While such an extract would kill mice, so would a similar extract of a non-toxic control fish *Pristipomoides microlepis* (Bleeker), although at a higher dose-level. Satisfactory differentiation of toxic and non-toxic fish could be achieved with a more highly purified extract. The initial ethanolic extract of dried fish flesh was concentrated *in vacuo* and diluted with thrice its own volume of water. The resulting solution was first extracted with light petroleum, then with ether. The bulk of the toxin was found in the ethereal extract. This extract after removal of the solvent when injected intraperitoneally into mice (closed colony Carworth Farms Webster strain, weighing between 19 and 21 gm.) would produce kills at a level of 0·2 mgm./gm. while the ethereal extract of the control fish caused no symptoms at a level of 1·5 mgm./gm. The results of these experiments are included in Table 1.

Table 1. Comparison of Bioassay Methods

	Water extract (5 mice used for each specimen)	Intraperitoneal injection in mice: Diethyl ether extract, in mgm. extract/gm. mouse. Figures represent mean time to death in min. of two mice tested at each level					
		0·1	0·3	0·5	0·7	1·0	1·5
Specimen (*Lutjanus bohar*)							
Highly toxic							
1	N.D.*	(3488)†	189	130	93	‡	
2	N.D.	(1,627)	249	155	111	69	89
3	N.D.	N.D.	240	81	90	43	30
4	N.D.	(360)	90	44	63	62	43
5	N.D.	N.D.	261	139	78	72	49
6	N.D.	308	128	101	89		
Moderately toxic							
7	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	
8	N.D.	N.D.	788	850	108	—	
9	N.D.	N.D.	(2,800)	750	—	124	
10	N.D.	N.D.	—	N.D.		(367)	
11	N.D.	N.D.	N.D.	1,252		1,044	
12	N.D.	N.D.	N.D.	(1,620)	—	—	
Non-toxic							
13	N.D.	N.D.	N.D.	N.D.		2,800	
14	N.D.	N.D.	N.D.	N.D.		N.D.	
15	N.D.	-	N.D.	N.D.	N.D.	N.D.	N.D.
16	N.D.		N.D.	N.D.	N.D.	N.D.	1,080
17	N.D.		N.D.	N.D.	N.D.	N.D.	
Pristipomoides microlepis (Control)	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.

* N.D. signifies no deaths in the 72-hr. test period.
† Figures in parenthesis are times to death in one mouse of pair tested, the other living through test period.
‡ Dash indicates no tests made at this level.

While sufficient amounts of toxic extract for injection of larger numbers of animals have not been available for a quantitative bioassay, the assay method described above allows reliable recognition of ciguatera toxin. Further research aimed at the isolation and identification of the pure toxin is in progress.

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Albert H. Banner
Satoshi Sasaki
Philip Helfrich
Charles B. Alender
Paul J. Scheuer*

Hawaii Marine Laboratory,
University of Hawaii,
Honolulu 14, Hawaii.

* Department of Chemistry, University of Hawaii.

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Properties of Vessel Muscle Proteins extracted with Water or Salt Solutions of Low Ionic Strength

Earlier investigations on the relations of the electrolyte content of organs to hypertension in the rat have shown that only the increase of the potassium content of the vessel wall is characteristic of hypertension[1]. In the carotic strip of cow *in vitro*, potassium produces a rise in tension which lasts so long as the potassium concentration of the bath solution is not altered. Simultaneously with the penetration of potassium into the muscle fibre a rise in tension[2], viscosity and dynamic elasticity modulus[3] occurs. It may be concluded from this that the potassium which entered the muscle fibre discharges certain proteins and so increases the mechanical tension.

Starting from this hypothesis, I have made extracts of relaxed vessel muscles using water or salt solutions of ionic strength either lower than that in the intracellular fluid or equal to it. The muscle of the relaxed cow carotis was separated from other tissues. Then it was minced in a small meat grinder, mixed in a mortar for 10 min. at room temperature with 1·5 c.c./gm. of the chosen solution and finally centrifuged for 15 min. at 22,000*g*. Extracts so obtained have a high viscosity (η rel. = 6·02 at a protein concentration of 1·55 per cent; extract of striated muscle of the same animal η rel. = 1·61 at a protein concentration of 1·67 per cent) and show double refraction of flow. After addition of 0·6 *M* potassium chloride (*p*H 7·0) at 15–18° C., they turn into a more or less thixotropic gel after a few seconds. The gelling also takes place, but more slowly, at lower potassium concentrations so long as these exceed that in the intracellular space. Extracts prepared by the same procedure from striated muscle of the cow, rabbit or rat and from smooth muscle of the non-pregnant uterus, bladder and small intestine of the rabbit or the small intestine of the rat do not show the above-mentioned properties. (Extracts of smooth muscle of the bladder and small intestine of the cow show double refraction of flow.) This can be taken as a hint that the vessel muscle contains, besides actomyosin, other structure proteins which are responsible for the permanent tension. We have, therefore, in collaboration with Hamoir, investigated extensively vessel muscle extracts by electrophoresis and ultracentrifugation. The results of these investigations will be reported in another communication.

Our findings clearly demonstrate the presence of two structure proteins. The study of their solubility has enabled us to isolate these proteins and to investigate them separately, as well as the actomyosin which was isolated from the vessel muscle.

L. Laszt

Department of Physiology,
University of Fribourg,
Fribourg, Switzerland.

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Conjugation of *p*-Aminohippurate by the Kidney and Effective Renal Plasma-flow

The clearance of *p*-aminohippurate has become the standard method for the determination of effective renal plasma-flow, with the assumption that there is no conjugation of *p*-aminohippurate during its passage through the kidney from the blood to the urine. The metabolism of this substance in the body is considered to be similar to that of sulphanilamide which it resembles, namely, acetylation of the *para* amino group. *p*-Acetylaminohippurate and *p*-aminohippurate have similar clearances in the dog and man, so the former may be expected to depress maximal tubular excretion of the latter, but as neither *p*-acetylaminohippurate nor any metabolite in which the *para* amino group is substituted is estimated by the technique used for *p*-aminohippurate, conjugation at sites other than in the kidney should not affect the clearance of the latter. With sulphanilamide, conjugation occurred only in the liver of rabbits and rats, in the liver and spleen in cats, and not at all in the dog (cf. ref. 1). *p*-Aminohippurate itself was not conjugated by rabbit[2] or dog[3] kidney slices *in vitro*, although some conjugation was found with rat[4] and guinea pig[2] kidney slices. From the evidence available, Smith[1] came to the conclusion that conjugation in the kidney did not occur to any significant extent in the species studied (rat, rabbit, cat, dog and man), although it has been suggested by others that conjugation could explain low clearances of *p*-aminohippurate with falling plasma concentrations in man[5].

It will be seen from Table 1 that the conjugation of *p*-aminohippurate does occur to an appreciable extent in the kidney of a number of species; 95 ± 1·3 per cent (22 observations) was recovered after mild acid hydrolysis (100° C. for 30 min., final acid concentration 0·56 *N*). The findings in the rabbit agree with earlier reports, but in the cat only low rates were found in the liver and none demonstrable in the spleen. That this conjugation did interfere significantly with the determination of effective renal plasma-flow was shown in the guinea pig, in which the clearance of free + conjugated *p*-aminohippurate was 1·19 ± 0·05 ($P < 0.01$) (9 determinations) times that of free *p*-aminohippurate on the same samples, with a mean plasma concentration of 0·10 ± 0·015 μmole free *p*-aminohippurate/ml. At this concentration, the calculated values for conjugation and excretion give a value of 1·17 for the above ratio, if the clearance of *p*-aminohippurate is taken to be 13 ml./min. (the mean value of the 9 determinations) and the kidneys weigh 4 gm. each.

The rate of conjugation *in vitro* was maximal at 0·1 μmole/ml., so less error would probably be introduced at higher plasma concentrations, although

Table 1. CONJUGATION OF *p*-AMINOHIPPURATE *in vitro* BY TISSUE SLICES

Approximately 100 mgm. tissue was incubated for 3 hr. in 2·3 ml. medium containing 30 μmoles sodium acetate in place of an equivalent amount of sodium chloride and 0·4 μmole sodium *p*-aminohippurate. Values given are means with standard errors with numbers of slices and animals used in brackets

Medium and species	*In vitro* conjugation in μmole gm. fresh weight/hr.		Estimated *in vivo* excretion of *p*-aminohippurate by kidney in μmole/gm./hr. at a plasma concentration of 0·1 μmole *p*-aminohippurate/gm./hr.	Values used for calculation of estimated *in vivo* excretion	
	Liver	Kidney		*p*-Aminohippurate clearance	Weight of both kidneys
Tris saline (ref. 6)					
Guinea pig		1·31 ± 0·02 (2,1)			
Cross and Taggart medium (ref. 2)					
Guinea pig	0·24 ± 0·01 (2,1)	1·14 ± 0·08 (16,5)	9·8	13 ml./min.	8 gm.
Mouse (white)	0·28 ± 0·03 (2,1)	0·83 ± 0·21 (4,2)			
Rabbit	0·41 ± 0·03 (2,1)	< 0·05 (6,2)	15	2·50 ml./gm. kidney (ref. 1)	
Cat	0·07 ± 0·01 (2,1)	< 0·05 (2,1)		4·09 ml./gm. kidney (diodrast) (ref. 7)	
Cow	0·15 ± 0·01 (2,1)	0·54 ± 0·02 (2,1)	24		
Pig	0·18 ± 0·01 (2,1)	0·35 ± 0·02 (2,1)	20	19·5 ml./kgm. body-weight (ref. 8)	1·17% of body weight
Sheep	0·42 ± 0·05 (3,2)	0·76 ± 0·04 (3,2)	13	500 ml./min. (ref. 9)	225 gm.

No significant conjugation was seen with slices of spleen, lung or heart muscle of any of the species.

the concentration at which maximal tubular excretion is of importance must be kept in mind. At concentrations less than 0·1 μmole/ml., the rate of *in vitro* conjugation fell with the concentration, so the error introduced would probably be similar to that of about 20 per cent found at 0·1 μmole/ml.

For the species which do conjugate *p*-aminohippurate in the kidney, a truer value for effective renal plasma-flow would probably be obtained by determining the clearance of free + conjugated *p*-aminohippurate or of *p*-acetylaminohippurate alone.

B. P. SETCHELL
E. BLANCH

Veterinary Research Station,
Glenfield, New South Wales.

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Enzymatic Reduction of the Yellow Pigment of *Drosophila*

IT has been demonstrated that the enzymatic conversion of dihydrofolic acid to tetrahydrofolic acid plays an important part in various biochemical reactions[1–3]. It has also been suggested that 7,8-dihydropteridine is reduced to the tetrahydro-level by the enzyme extracted from sheep liver in the presence of reduced triphosphopyridine nucleotide[4]. Recently, the yellow pigment (sepiapterin[5]) of *Drosophila* has been confirmed to be 2-amino-4-hydroxy-6-lactyl-7,8-dihydropteridine[6]. It was therefore thought that the yellow pigment of *Drosophila* might be also converted to tetrahydropteridine by the enzyme extracted from liver.

The dihydrofolic acid reductase from chicken liver was prepared by Futterman's method[7]. It was found that the reductase attacked 2-amino-4-hydroxy-6-lactyl-7,8-dihydropteridine and extinguished both the yellow colour and yellow fluorescence of its solution in the presence of reduced triphosphopyridine nucleotide, but not of reduced diphosphopyridine nucleotide as shown in Fig. 1. The reaction gave a product with a spectrum characteristic of tetrahydropteridine. Thus, this enzyme is capable of reducing the dihydropteridine as well as dihydrofolic acid to 5,6,7,8-tetrahydropteridine with reduced triphosphopyridine nucleotide.

By auto-oxidation, a great portion of the enzymatic reaction product (5,6,7,8-tetrahydropteridine) was converted to a completely dehydrated form having a blue fluorescence, and a small portion was reversed to a partially dehydrated form, namely, the original dihydropteridine, having a yellow fluorescence. The former compound was easily converted to 2-amino-4-hydroxypteridine-6-carboxylic acid by photo-decomposition or oxidation with potassium permanganate. Furthermore, it was decomposed to the same carboxylic acid and aceto-aldehyde by periodate. From these results, it was assumed that the blue fluorescent substance carried the same substituent in the 6-position as that of the original dihydropteridine. Thus, the substance is presumed to be 2-amino-4-hydroxy-6-lactyl-pteridine.

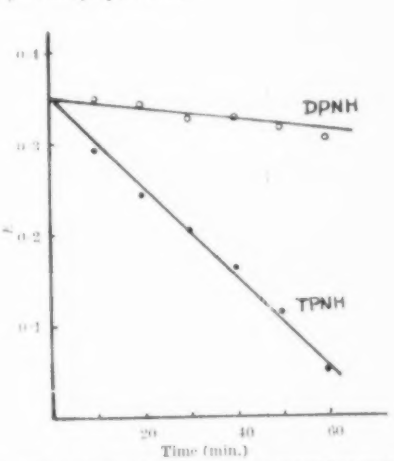

Fig. 1. Effects of reduced tri- and di-phosphopyridine nucleotides on dihydropteridine reductase. Reaction mixture: 10 μgm. 2-amino-4-hydroxy-6-lactyl-7,8-dihydropteridine; 40 μgm. reduced tri- or di-phosphopyridine nucleotide; 45 m*M* phosphate buffer *p*H 6·0; 0·3 ml. chicken liver enzyme fraction. Total volume 3 ml. Temperature of incubation 37° C. A spectrum characteristic of the dihydropteridine at 410 mμ

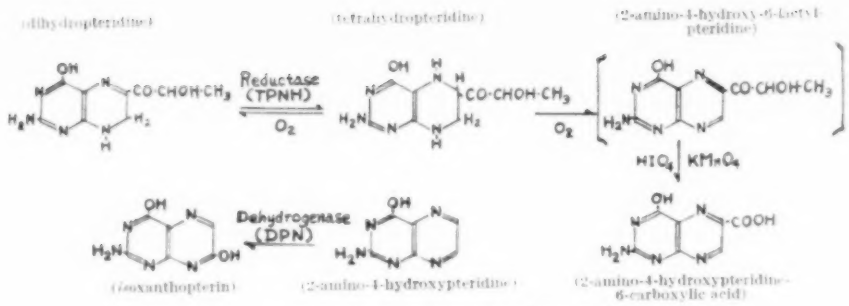

Fig. 2. A possible metabolic pathway of pteridines in *Drosophila*

The product in the enzymatic reaction mixture contained a considerable amount of *iso*xanthopterin that was not present in the original reaction mixture. I confirmed that the chicken liver extract was capable of converting 2-amino-4-hydroxypteridine to *iso*xanthopterin. Therefore, it is suggested that 2-amino-4-hydroxypteridine was derived from the decomposition of tetrahydropteridine and converted enzymatically to *iso*xanthopterin.

In the presence of reduced triphosphopyridine nucleotide, the partially purified enzyme of *Drosophila* was capable of reducing the dihydropteridine to the tetrahydropteridine from which 2-amino-4-hydroxytryptamine can be derived by auto-oxidation. It has been shown that the latter can be converted to *iso*xanthopterin by pteridine oxidase[6] or dehydrogenase[7] extracted from *Drosophila*. These observations suggest a metabolic pathway of pteridines in *Drosophila* such as is shown in Fig. 2.

Toshifumi Taira

National Institute of Genetics,
Misima, Sizuoka-ken,
Japan.

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Cardiac Effects of Streptolysin O in Rabbits

Although several of the known streptococcal enzymes or toxins have been suspected of playing a part in the pathogenesis of the heart lesions in rheumatic fever, a number of reports have suggested that streptolysin *O* may be of some importance in the causation of focal cardiac damage in experimental animals. Kellner *et al.*[1] have demonstrated that the rabbit heart *in vitro* is extremely sensitive to this substance. Schwab *et al.*[2], among others, showed that rabbits pre-treated with certain streptococcal factors developed a high incidence of focal cardiac lesions on subsequent injection of streptolysin *O* containing filtrates. These investigations were carried out with impure preparations of unknown complexity.

Previous reports from this laboratory have described the value of agar precipitin analysis in the study of human streptococcal infections[3–5]. In the course of this work, very highly purified streptolysin *O* preparations were obtained, using a combination of continuous-flow electrophoresis and column chromatography on calcium phosphate (hydroxylapatite) gels. Sufficient amounts of similar preparations from a group *A* and group *C* streptococcal strain have been separated in order to study their effects on intravenous injection in rabbits. Such observations were made in an attempt to translate the above-cited findings to the *in vivo* environment. Although the final fractions were not as free of contamination immunologically as those obtained previously[5], they were both extremely potent. The group *A* fraction revealed about 160,000 hemolytic units/mgm. protein, and the group *C* about 60,000 units/mgm. Both contained small amounts of diphosphopyridine nucleotidase, and the group *A* showed traces of a third component immunologically. The group *C* material, only, contained appreciable amounts of apparently non-protein substances in the lyophilized powder (about 40 per cent).

The cardiotoxic effects of intravenously injected streptolysin *O* in rabbits were studied electrocardiographically in all instances. In a number of cases, femoral artery blood pressures and electroencephalograms were also recorded. Albino rabbits from a single dealer (2·6–3·2 kgm.) of either sex were used. The streptolysin solutions, and all others, were made in 0·1 *M* sodium phosphate at *p*H 7·2. Activation of the streptolysin was carried out by adding a neutralized L-cysteine hydrochloride solution to a final concentration of 10 mgm./ml., and incubating at 30° C. for 10 min., following which it was kept in an ice-bath.

The *LD*50 of the group *A* activated (reduced) streptolysin was approximately 0·15 mgm. dry weight of the lyophilized powder, while that of the group *C* material was 0·75 mgm. dry weight (about 0·45 mgm. protein). A total of 50 rabbits was used for these assays.

Following injection, with few exceptions, death ensued within 5 min., or less, associated with convulsions and respiratory standstill. It was observed that considerable electrocardiographic changes always preceded the convulsions, and could be produced within as short a time as 3 sec. with 3–4 *LD*50. The injection itself took approximately 2–3 sec. Examples of the very rapid electrocardiographic changes are shown in Figs. 1*a* and *b*. There was immediate transition from normal sinus rhythm to ventricular arrhythmia, followed by electrocardiographic silence.

With smaller but still lethal doses (1–2 *LD*50) the reaction often took somewhat longer to develop. An

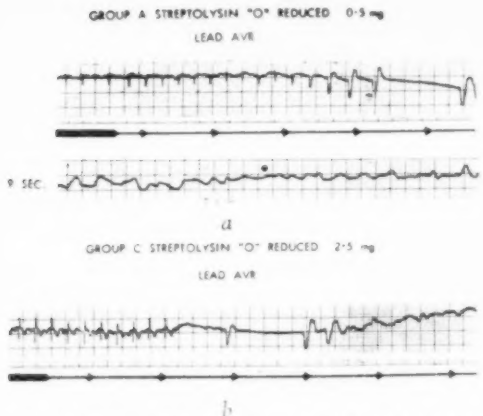

Fig. 1. Electrocardiographic tracings of rabbits receiving intravenous injections of reduced activated streptolysin *O* in several multiples of the *LD*50 dose. The injection period is marked on the 1-sec. time interval record. *a*, Group *A* streptolysin *O*, 0·5 mgm. dry weight/0·5 ml. (Lower strip tracing starts 9 sec. after the injection was completed.) *b*, Group *C* streptolysin *O*, 2·5 mgm. dry weight/1·0 ml.

example of the electrocardiographic changes occurring in a rabbit receiving such a dose of the group *A* preparation is shown in Fig. 2. Within 25 sec., unifocal ventricular rhythm with ST segment depression occurred. Within 125 sec., typical ventricular arrhythmia was seen, and within 224 sec., ventricular tachycardia was soon followed by ventricular fibrillation. In all instances, the motor convulsions occurred without electroencephalographic convulsive discharges.

In nine of thirteen cases, non-lethal doses of the fractions produced temporary electrocardiographic changes, such as ST—T depression, supraventricular or ventricular extrasystoles, or bigeminal rhythm, but these were erratic in occurrence. Sometimes they lasted intermittently at least as long as 18 hr.

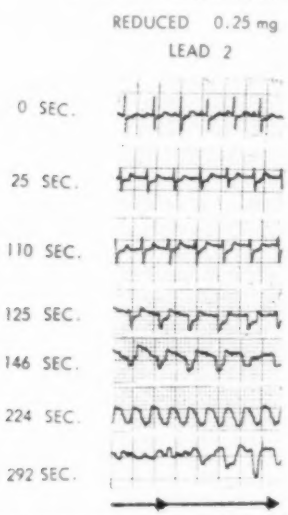

Fig. 2. Electrocardiographic tracings of a rabbit receiving an intravenous injection of about one *L*100 dose of reduced activated group *A* streptolysin *O*. The elapsed times following the completion of the injection are recorded

When lethal doses were given, the blood pressure dropped rapidly to less than 25 mm. mercury. This fall occurred either following or prior to the electrocardiographic changes, and was later followed by electroencephalographic silence.

Evidence that the lethal effects were due to streptolysin *O* was obtained in several ways, in addition to the high degree of apparent purification immunologically. Much larger doses of the reversibly oxidized inactive form were required to bring about lethal effects, 1 mgm. dry weight of the group *A*, and 6·5 mgm. of the group *C* preparations being required. The time required for death was substantially longer with the oxidized form as compared to equivalent amounts of the reduced. It is likely that the streptolysin may be gradually reduced to activity *in vivo* in view of the known oxidation-reduction potential of tissues[8].

Cholesterol, a potent inhibitor of the haemolytic activity of streptolysin *O* (ref. 7), protected rabbits against the lethal and electrocardiographic effects, when an aqueous suspension was mixed with the challenge dose. Diphosphopyridine nucleotidase has been shown to be unaffected by cholesterol, and by reduction with cysteine[8].

Numerous control experiments with cysteine, and different streptococcal fractions previously isolated[9], including deoxyribonuclease *B*, streptococcal proteinase, C-carbohydrate protein complex[9], and an antigen possibly related to scarlet fever toxin, failed to produce similar electrocardiographic effects. *Shigella paradysenteriae* Flexner type III endotoxin also did not show any such reactions.

These observations showed that streptolysin *O* from a group *A* and a group *C* streptococcal strain may kill rabbits extremely rapidly when given intravenously. Extensive electrocardiographic and blood pressure changes were observed preceding death. With several multiples of the lethal dose, cessation of cardiac activity was noted within 3·5 sec. following the injection. The findings presented here support the speculation that streptolysin *O* may be the factor causing cardiac lesions *in vivo*, as a result of repeated streptococcal infections in experimental animals (for example, ref. 10). Their relation to the pathogenesis of human rheumatic fever remains to be determined.

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S. P. Halbert
R. Bircher
E. Dahle

Departments of Microbiology and Pharmacology,
College of Physicians and Surgeons,
Columbia University, New York.

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Levels of Serotonin during Convulsion and the Effect of Reserpine

In view of the contradictory reports[1-3] with respect to changes in the 5-hydroxytryptamine (5-HT) levels of the mammalian central nervous system during convulsion, this problem was re-examined in rats in which convulsion was induced by intraperitoneal injection of fluoroacetate or 'Metrazol'. The former convulsant was particularly preferred because, unlike the convulsive agents generally employed, its action can be related to specific biochemical events, that is, blocking of the citric acid cycle[4] with concomitant changes in certain amino-acid[5]- and ammonia[6]-levels of the central nervous system.

The serotonin content of brain, small intestine and spleen of rats treated with convulsants, with or without simultaneous administration of reserpine, was compared with control animals. The solution of reserpine for intraperitoneal injection was prepared by dissolving reserpine crystals (100 mgm.) in 0·1 ml. of concentrated formic acid, 2·5 ml. propylene glycol, 2·5 ml. absolute alcohol and water to make the volume 20 ml. (Formate was used instead of glacial acetic acid to avoid the competition of acetate with fluoroacetate.) The animals which did not receive reserpine received only intraperitoneal injection of reserpine solvent. The animals were killed at 60 min., with the onset of convulsion at 30 min. The amount of fluoroacetate injected was greater than the *LD*50, 5 mgm./kgm. for rats, in order to ensure the severity and the recurrence of seizures between onset and time of killing.

Statistical analysis of the values in Table 1 indicates that fluoroacetate-produced convulsion does not cause an increase of serotonin-level in the brain or in the other organs analysed. Administration of reserpine did not produce any delay in the onset of convulsions or in the incidence of seizures. However, it depleted serotonin within 1 hr. by 78 per cent from the brain of convulsing animals, but not from the spleen or the intestine, a pattern similar to that produced by reserpine in non-convulsing rats[6]. Administration of reserpine did not alter the fluoroacetate-produced citrate accumulation in the brain to any degree of statistical significance. In another series of experiments 'Metrazol' (60 mgm./kgm.) was administered intraperitoneally alone and with reserpine. 'Metrazol', like fluoroacetate, had no effect on the 5-HT values of the brain of convulsing rats killed 1 hr. after administration of the drug. Again, convulsions produced by 'Metrazol' had no effect on the release of 5-HT by reserpine from the brain.

It can safely be stated that there is no statistically proved evidence to demonstrate that fluoroacetate, and, under the conditions of our experiments, 'Metrazol', have any effect on the 5-HT levels of rat brain.

Table 1. Effect of Convulsion on 5-Hydroxytryptamine Content of Some Rat Tissues and the Influence of Reserpine. Sprague–Dawley male rats (350–400 gm.) received intraperitoneally sodium fluoroacetate (8 mgm./kgm.) and reserpine (6 mgm./kgm.) as indicated. 5-Hydroxytryptamine was determined by the spectrophotofluorometric method (ref. 7) and the citrate, as described elsewhere (ref. 4). Numbers of animals indicated in brackets

Group	5-Hydroxytryptamine (μgm./gm. wet tissue) Brain	Spleen	Small intestine	Citrate (μgm./gm. wet tissue) Brain
Control (10)	0·41 ± 0·03*	2·02 ± 0·22	2·08 ± 0·30	19 ± 1·3
Fluoroacetate (10)	0·48 ± 0·03	1·78 ± 0·27	2·11 ± 0·36	151 ± 10
Fluoroacetate + reserpine (10)	0·11 ± 0·05	1·90 ± 0·28	2·30 ± 0·30	119 ± 13
Reserpine (5)	0·12 ± 0·05	2·34 ± 0·67	3·00 ± 0·39	
'Metrazol' (6)	0·40 ± 0·02	2·17 ± 0·18	3·43 ± 0·31	
'Metrazol' + reserpine (6)	0·25 ± 0·05	2·40 ± 0·25	3·16 ± 0·26	

* *S.E.*

E. M. Gal
P. A. Drewes
Neurochemical Research Laboratory,
Veterans Administration Hospital,
Sepulveda, California,
and
Department of Pharmacology,
School of Medicine,
University of California at Los Angeles.

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Enzymic Release of Sialic Acid and Inactivation of Human Menopausal Gonadotropin

It has been shown that the biological activity of chorionic and pituitary gonadotropins is lost when the hormone materials are treated with influenza virus or with receptor-destroying enzyme[1-3]. This enzyme has been recognized as neuraminidase[4], and the loss of biological activity of gonadotropins on treatment with the above catalytic agents was accompanied by the release of sialic acid. It seemed desirable to investigate the effect of neuraminidase on the chemical composition and biological activity of a purified preparation of human menopausal gonadotropin[5,6].

The relative potency of the preparation used, in terms of human menopausal gonadotropin-24, was 100 when tested by the augmentation of uterus weight in 3-week-old female mice. It contained 7·8 per cent of sialic acid, determined by the diphenylamine reaction[7] and expressed as N-acetylneuraminic acid. Heating at 100° C., *p*H 2, for 1 hr. destroys the activity and quantitatively removes sialic acid, but it is possible that other bonds (sugar, amino-acid) were broken.

10 mgm. of human menopausal gonadotropin preparation, dissolved in 10 ml. *M*/15 phosphate buffer, *p*H 6·3, was incubated with about 30,000 units of neuraminidase (receptor-destroying enzyme, Behringwerke) at 35° C. After 24 hr. the solution showed a loss of gonadotropic activity of 80 per cent, as compared with a control kept under the same conditions but without the receptor-destroying enzyme. Reaction mixture was then dialysed twice against 10 vol. of water at 0° for 48 hr. About 60 per cent of initial sialic acid was found in the dialysate. After concentration, the dialysate was applied to a column of 'Dowex 2' 200–400 mesh (20 × 0·8 cm.), equilibrated in 0·1 *M* formic acid[8]. The effluent was collected in 3-ml. fractions which were analysed for their sialic acid content. Elution with 0·3 *M* formic acid yields two peaks (fractions 13–19 and 24–29).

Paper chromatography (*n*-butanol / pyridine / 0·1*N* hydrochloric acid, 5 : 3 : 2) showed that the two peaks contained the same component which was identified as *N*-glycolylneuraminic acid. Release of glycolic acid, after hydrolysis by *N* sulphuric acid, confirmed this result[9].

Although the human menopausal gonadotropin preparation was not pure, the following conclusions may be drawn from the experimental results: (*a*) human menopausal gonadotropin contains sialic residues which are accessible to neuraminidase; (*b*) enzymic release of the sialic acid residues reduces the biological activity of human menopausal gonadotropin by 80 per cent or more. Bound sialic acid is an essential part of the molecule.

René Got
Roland Bourrillon

Laboratoire de Biochimie,
Faculté de Médecine,
45 rue des Saints-Pères,
Paris 6.

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Seasonal Variation in Blood Pressure in Man

Several of man's bodily functions, such as thyroid activity, are known to show a characteristic seasonal pattern; but in general such seasonal variations have received less attention in man than in many other animals. In particular, seasonal trends in blood pressure do not seem to have been measured hitherto.

The data presented here were derived from measurements on 56 middle-aged men who had been observed for 1–3 years at a clinic for ischæmic heart disease. Most had suffered cardiac infarction, but for all of them at least two months had elapsed since the acute illness and during the period of observation they were in a clinically stable state. There were three observers, but as a rule each subject's blood-pressure measurements had all been taken by the same observer. All measurements were made in a comfortably warm room after a period of rest and using standard instruments.

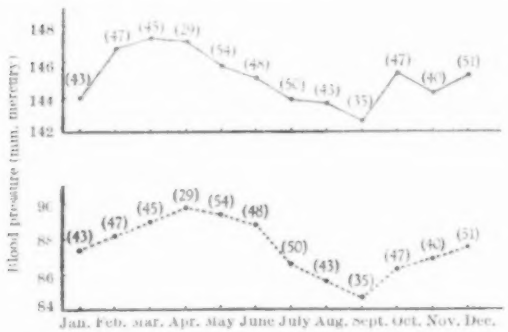

Fig. 1. Mean systolic (above) and diastolic (below) blood pressures, by months, of 56 men. (No. of observations are shown in brackets)

The results are shown in Fig. 1, where mean systolic and diastolic pressures have been plotted by months; the technique of grouped means has been followed; the value at each month represents the mean of the values for that and the two adjacent months. There is a clear seasonal trend, with a peak covering the spring and a trough in the late summer.

This pattern is quite different from that of ischæmic heart disease morbidity and mortality, which follow the reciprocal of air temperature, namely, a peak in January and February and a lower level throughout the late spring and summer.

Geoffrey Rose

Department of Epidemiology,
London School of Hygiene and Tropical Medicine,
Gower Street, London, W.C.1.

Relationship between Urinary Hyaluronidase and Diuresis

In a recent communication, Berlyne[1] states that he was unable to corroborate my results[2] on the relationship between the hyaluronidase activity of the urine and diuresis.

(1) Berlyne believes that my method is unsuitable for quantitative assay of urinary hyaluronidase, as I did not take into account the drop of substrate viscosity before the first reading. But the determination of enzyme activity by the method of Swyer and Emmes[3], used by me, does not depend on the initial substrate viscosity. The modified method of McLean and Hale[4], used by Berlyne, has no advantage over mine.

He thinks that my results are not precise enough because I did not take into account the electrolyte effect. But in practice I did take it into consideration, and some of my experiments were performed on samples of urine previously dialysed. On the removal of electrolytes, hyaluronidase activity somewhat increases. But the correction introduced by dialysis does not alter the main relationship and curves of dialysed urine, as well as of electrolyte-containing urine run in parallel[5].

(2) Berlyne believes that I was wrong when giving the results as the fermentation activity of the urine in arbitrary units. In his opinion, the results should be expressed by the amount of the enzyme excreted per minute. I cannot agree with this.

The urinary hyaluronidase is produced by renal cell secretion under the action of antidiuretic hormone. The enzyme performs a specific function in the kidney. It depolymerizes hyaluronic structures of the tubules, and this provides the conditions for antidiuretic reaction. The appearance of hyaluronidase activity in urine should not be regarded as a process of excretion. This phenomenon is merely a side-effect of the antidiuretic hormone enabling one to verify the mechanism of the hormone action.

From the above point of view, there is no reason to express the results as the product of the enzyme concentration (irrespectively of any units) by the volume of urine, as it is done for estimating the excretion of substances removed by the kidney. As this operation has no physiological meaning in this case, it becomes purely arithmetical and completely distorts the essence of the phenomenon under study.

(3) The probability of my physiological interpretation of the phenomenon in question was investigated in two series of experiments. In one (jointly

with V. Vasiljeva and J. Natochin), dogs were decerebrated, the cut running behind the tuber cinereum. The hypophysis was removed and the kidney denervated. To maintain a steady diuresis-level, minotol solution was administered intravenously. A few urine samples were collected for 1 hr. Then a large dose of 'Pitressin' was injected, and urine was collected for another hour.

On the removal of antidiuretic hormone-producing structures, urine, unlike normal dog urine, does not exhibit hyaluronidase activity during osmotic diuresis. Under the hormone action, the enzyme appeared in urine in spite of the fact that urine flow increased.

In another series of experiments (jointly with L. Ivanova) on dogs with a permanent fistula of the ureter, the animals were deprived of water for 24 hr. Urine collected during hydropeny revealed high hyaluronidase activity. The second urine sample was collected after the dog was allowed to drink water and then diuresis exceeded 1 ml. per min. In this sample no enzyme was found. Then urine was concentrated in vacuum. Thus it was artificially reduced to the volume corresponding to the rate of natural urine flow during dehydration. Yet even then the urine did not acquire hyaluronidase activity. Thus the loss of enzyme at water diuresis cannot be accounted for by the dilution alone, though this factor certainly exercises its usual effect.

(4) The difference between osmotic and water diuresis is particularly distinct if the corresponding correction eliminates the dilution effect. I did this in the following way. Urine samples collected at different levels of diuresis were dialysed and then concentrated in vacuum to the volumes corresponding to a urine flow of 0·2 ml./min. In this way I obtained the results shown in Fig. 2 of my communication in *Nature* to which Berlyne refers. All the points on the curve, both for water and osmotic diuresis, represent urine activity under reduced conditions. Hence the results are not complicated either by dilution or by electrolyte effect. Considering the process under such constant conditions, I arrived at the conclusion that secretion of hyaluronidase by renal cells decreases during water diuresis, but it remains at a constant level during osmotic diuresis.

By direct estimation of hyaluronidase activity of urine collected during osmotic diuresis without any correction for dilution, I certainly found that activity drops as the flow of urine increases.

A. G. Ginetzinsky

Sechenov's Institute of Evolutionary Physiology,
Academy of Sciences of the U.S.S.R.,
Staropargolovsky 52,
Leningrad, *K*-21.

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I am grateful for the opportunity afforded by Prof. Ginetzinsky's letter to clarify certain points in my previous communication[1] which I had omitted as they are dealt with at length elsewhere[2]. I hope to resolve some of the problems mentioned by Prof. Ginetzinsky point by point.

(1) It has been shown by McLean and Hale[3] and confirmed by me[1,2] that the ionic strength of the hyaluronic acid – buffer – hyaluronidase system must be kept constant if quantitative measurement of hyaluronidase is to be achieved. In a system containing constant amounts of hyaluronidase and hyaluronic acid, as the ionic strength of the medium is increased from 0 to 0·3 *M* the apparent hyaluronidase activity changes from 0 to 90 units (Fig. 3 of ref. 3). Thus it is essential to control electrolyte concentration carefully if quantitative results are to be obtained with urine. I chose to keep ionic strength constant by electrometric estimation and addition of salt in appropriate amounts rather than use dialysis, where adsorption of hyaluronidase might take place on to the dialysing membrane. The method used is published in detail elsewhere[2].

(2) It seems reasonable to express urinary hyaluronidase findings in terms of excretion per unit time, as is the practice with other urinary solutes. If one accepts the statement that hyaluronidase appears in the urine "merely as a side-effect of the antidiuretic hormone" and "not as a process of excretion" in order to justify the use of hyaluronidase concentration as opposed to excretion per minute, then there is little point in measuring hyaluronidase excretion (either per ml. or per min.) as evidence for or against Ginetzinsky's hypothesis of the role of hyaluronidase in the urine-concentrating mechanism. If one plots urinary hyaluronidase concentration against urine flow, one obtains a similar graph to that which would be obtained by plotting creatinine concentration against urine flow; that is, the lower the flow, the higher is the concentration of both hyaluronidase and creatinine. Nobody would suggest that creatinine is implicated in the antidiuretic hormone mechanism of urine concentration, yet Ginetzinsky used evidence of this type to suggest that hyaluronidase is instrumental in the antidiuretic hormone mechanism for urine concentration.

(3) I am not familiar with the decerebrate hypophysectomized dog preparation and am unable to comment on this experiment without knowing details of urine electrolyte concentration, urine flow-rate, etc. In Ginetzinsky's article (ref. 4, Fig. 2) he shows that the dog in osmotic diuresis in four out of five results has urine flows of 1·5 ml./m.²/min. or less. These are very small for adequate mannitol osmotic diuresis, and are not strictly comparable with my results in humans, where urine flows up to 9·5 ml./min. were reached.

The fact that Prof. Ginetzinsky in only some experiments dialysed and then reduced to constant volume indicates that he realized the need for measuring hyaluronidase excretion per min. Unfortunately, he did not do this in all experiments; hence his results are not uniformly expressed and therefore direct comparisons cannot be made.

Since my initial communication I have extended the number of observations on humans in water

Table 1

Urine (ml./min.)	Osmolality of urine (mOsmols/kgm.)	Hyaluronidase (units/ml.)	Hyaluronidase excretion per min.
3·42	240	0·6	2·04
4·2	133	0·25	1·1
4·75	154	0·45	2·1
5·6	162	0·38	2·1
6·23	91	0·75	4·7
6·7	104	0·45	3·0
7·8	94	0·125	0·98
8·06	103	0·26	2·1
9·55	84	0·12	1·2
10·7	55	0·12	1·3

diuresis in the range 3·42–10·7 ml./min., as shown in Table 1.

It will be seen that I found detectable amounts of hyaluronidase even at high urine flows in water diuresis whereas Ginetzinsky does not. The most obvious explanation for this discrepancy is that I was using a more sensitive method, and one which does not involve loss from dialysis.

G. M. Berlyne

Department of Medicine,
The Royal Infirmary,
Manchester, 13.

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HISTOCHEMISTRY

Presence of Enterochromaffin Cells in the Gut of Amphioxus

Histochemical evidence has been found for the presence in the gut of amphioxus of argentaffin cells, which do not appear to have been described formerly; because of their localization and their histochemical characteristics, they can be considered to be of enterochromaffin type, shown to be present in other groups of Chordata (by Vialli and Erspamer[1] for all vertebrates, except Cyclostomata and Teleostea, and by Lison[2] for Ascidians).

The histochemical characteristics of typical enterochromaffin cells are well established[1], namely, positive reaction in the chromaffin, argentaffin and diazonium in alkaline solution tests. Other staining methods (non-histochemical) are also suitable for detection of enterochromaffin cells, based on their acidophilia and argyrophilia. Moreover, Jacobson[3] observed later that the specific substance fixed in the granules of enterochromaffin cells is removed by a hot pyridine–methanol mixture. Finally, quite recently, Pearse in his book[4] presents as characteristic of the enterochromaffin cells five major histochemical tests (chromaffin, argentaffin, diazonium, indophenol and Gibbs's reactions) and other subsidiary ones, including the autofluorescence, the Schmorl ferric–ferricyanide reaction and the Pearse thioindoxyl reaction.

For the present work, four specimens of *Branchiostoma lanceolatum* Pallas, 30–50 mm. long, after having been fixed in 10 per cent formol-saline and embedded in paraffin, were cut transversely to provide a series of sections of 6μ thickness.

In the gut, some cells were found to be strongly positive by the Masson–Hamperl argentaffin reaction. The argyrophil methods (particularly the Bodian reaction) gave also positive results, corresponding to those of the former reaction as regards number and localization of the cells. Positive results were obtained, however, with very faint contrast compared to the background, after the chromaffin reaction, the Gibbs indophenol reaction, the Lillie diazo–safranine reaction at *p*H 9·4 and the Schmorl ferric–ferricyanide reaction. No positive reaction was found with other diazo-coupling methods (with sulphanilic acid and stabilized diazonium salts), the Pearse thioindoxyl reaction or autofluorescence; after treatment with a pyridine–methanol mixture at 60° C. for five days, the sections did not stain with any of the methods mentioned above.

Fig. 1. Left wall of mid-gut; Masson argentaffin reaction. Epithelial ciliated cells are closely packed; some narrow enterochromaffin cells are seen. (× 500)

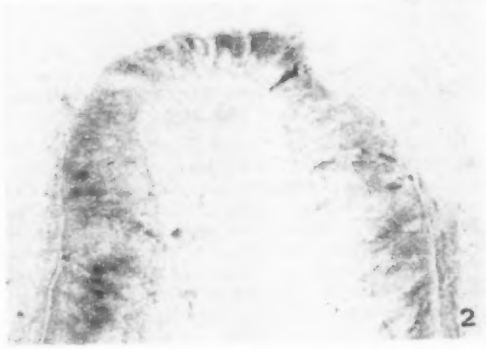

Fig. 2. Dorsal groove of hind-gut; Masson argentaffin reaction. Epithelial ciliated cells are less packed and narrow; one enterochromaffin cell is clear, but others are seen only with few granules in focus

The cells under examination are very slender in shape, occupying the whole height of the intestinal epithelium, and are slightly larger at the base, where the specific granules may be more evident. These cells are usually isolated, and not more than 5–8 occur in each section.

The enterochromaffin cells do not occur in the anterior tract of the digestive tube; they occur in the posterior part of the mid-gut on the left wall and the dorsal zone, to continue only dorsally in the ilio-colon ring and in the hind-gut. They are localized in the strongly ciliated tracts, that is, in the lateral ciliated tract of the posterior part of the mid-gut and the dorsal ciliated tract in the ilio-colon ring and in the hind-gut (the terminology corresponds with that of Barrington[5]). This peculiar distribution requires further study in connexion with the morphogenetic and functional interpretation.

I have not been able to find evidence for all the ordinary histochemical characteristics already mentioned for enterochromaffin cells of vertebrates, in which the presence of 5-hydroxytryptamine (enteramine) has been proved[6,7]; nevertheless, the failure of some tests may depend on decreased sensibility of the reactions, as has been confirmed in other cases, or on decreased contrast of the stain compared with the background. This problem was recently discussed by Vialli[8] in connexion with staining methods for enterochromaffin cells.

A more extensive investigation of this kind on which I am engaged should contribute to a unified interpretation regarding the biological meaning of the enterochromaffin system and the metabolism of 5-hydroxytryptamine, at least within the Chordata.

GIUSEPPE GERZELI

Istituto di Anatomia Comparata
e Centro di Studio per l'Istochimica del C.N.R.,
Università di Pavia.

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HÆMATOLOGY

Fibrinolytic Activities present in Human Blood Platelets

BLOOD platelets have been shown to contain antiplasmin activity[1–3]. The experiments to be described in this communication demonstrate that blood platelets interfere in still another way in fibrinolysis. The fibrinolytic activity brought about by streptokinase comprises two steps[4]: (1) activation of a proactivator which could be identical in man with plasminogen; (2) transformation of plasminogen to plasmin by the activator, resulting from reaction (1).

When human blood platelets are added in increasing concentrations to a test system composed of streptokinase and bovine fibrinogen, clotted by addition of thrombin–calcium solution, a progressive increase of fibrinolytic activity is observed. This was demonstrated by each of the following three methods: estimation of clot lysis-times, thrombelastographic recordings and the fibrin plate method according to Astrup and Mullertz[5]. Table 1 represents the results obtained with clot lysis-time determination.

Table 1. INFLUENCE OF HUMAN BLOOD PLATELETS ON STREPTOKINASE-INDUCED LYSIS OF BOVINE FIBRIN

Concentration of blood platelets in the added suspension	Clot lysis time
5,000,000/mm.³	15 min.
2,500,000/mm.³	21 min.
1,000,000/mm.³	40 min.
500,000/mm.³	85 min.
100,000/mm.³	18 hr.
Isotonic sodium chloride (control)	more than 48 hr.

0·1 ml. blood platelets suspension is mixed with 0·1 ml. streptokinase solution (1,000 U./ml.) and added to 0·5 ml. bovine fibrinogen (1 gm. per cent). The mixture is clotted by addition of 0·2 ml. Thrombin 20 U./ml., dissolved in *M*/20 calcium chloride. Determination of clot lysis-time at 37° C.

The bovine fibrinogen ('Rinderfibrinogen' from Behring-Werke, Marburg/Lahn, Germany) used as substrate contained large quantities of plasminogen but was nearly free of proactivator activity. In control experiments where blood platelets were substituted by isotonic sodium chloride solution, lysis did not occur within a 24-hr. period. The thrombin ('Test Thrombin' from Behring-Werke) used was found to be void of any appreciable contamination with plasminogen or proactivator. The streptokinase was a highly purified preparation, kindly supplied by Behring-Werke. Veronal buffer (*p*H: 7·35, μ: 0·154) according to Owren, was used for dissolving fibrinogen, streptokinase, urokinase and plasmin. Blood platelets were suspended in isotonic sodium chloride solution.

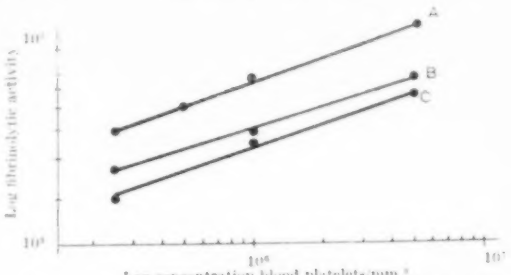

Fig. 1. Influence of washing platelets on their promoting effect on streptokinase-induced lysis of bovine standard fibrin. Results of determinations of fibrinolytic activity by the fibrin plate method. Double logarithmic graph. Abscissa: concentration of blood platelet suspension tested; ordinate: fibrinolytic activity as measured by the product of the two diameters of the lysed zones. The tested platelet suspension is mixed with an equal volume of streptokinase solution (5,000 U./ml.); 0·03 ml. of this mixture is placed on the surface of the plate. Curve *A*, blood platelets washed once with isotonic sodium chloride solution; curve *B*, platelets washed 5 times; curve *C*, platelets washed 10 times

The blood platelets tested in our experiments had been prepared by several techniques. Successively, lyophilized human blood platelets[6] and human blood platelets isolated from sequestrene, citrated or A.C.D. plasma were used. They all had a similar enhancing effect on streptokinase-activated lysis of bovine fibrin.

In contrast to the influence on streptokinase-induced lysis of bovine fibrin, human blood platelets had a clearly inhibiting effect on urokinase (kindly supplied by Dr. J. Ploug, Leo Pharmaceuticals, Ballerup, Denmark) or plasmin (the chloroform-activated bovine fibrinolysin, kindly supplied by Dr. E. Loomis, Parke Davis and Co., Detroit) activated lysis.

Further work showed that washing platelets resulted in a gradual weakening of the promoting effect on streptokinase-activated fibrinolysis. After ten washings, however, there was still an appreciable residual activity (Fig. 1). The antiplasmin effect, on the other hand, was only slightly diminished by the washing procedures.

Heating of platelets at 80° C. for 15 min. completely destroyed the above-described lysis-promoting activity. Instead of an enhancing an inhibiting effect on streptokinase-induced lysis was observed (Table 2). The antiplasmin activity was not diminished by this heating procedure.

Our results, which will be published in detail elsewhere, demonstrate that blood platelets, on addition of streptokinase, form an activator of plasminogen. This can be explained by the assumption that blood platelets contain so-called proactivator activity. The presence of plasminogen in blood platelets seemed to be ruled out as a possible explanation for the observed facts. Indeed, no fibrinolytic activity could be produced when mixtures of blood platelets and streptokinase were tested on heated fibrin plates, in which the plasminogen had been destroyed.

Table 2. INFLUENCE OF HEATING PLATELETS ON STREPTOKINASE-INDUCED LYSIS OF BOVINE FIBRIN

Concentration of lyophilized platelets in the added suspension	Clot lysis-time	
	Unheated platelets	Heated platelets (15 min. at 80° C.)
10 mgm./ml.	8 min.	120 hr.
2·5 mgm./ml.	18 ,,	72 ,,
0·625 mgm./ml.	42 ,,	46 ,,
Isotonic sodium chloride (control)	39 hr.	39 ,,

0·1 ml. lyophilized human blood platelets are mixed with 0·1 ml. streptokinase solution (5,000 U./ml.) and added to 0·3 ml. bovine fibrinogen (2 gm. per cent). This mixture is clotted by addition of 0·1 ml. thrombin (20 U./ml.) dissolved in *M*/10 calcium chloride. Determination of clot lysis-time at 37° C.

The investigation of the influence of washing and heating showed that the platelet proactivator is to be distinguished from the blood platelet antifibrinolysin. These two activities cannot be caused by an identical platelet substance. The lysis-promoting property of blood platelets completely masks their antifibrinolytic effect in the case of streptokinase-activated lysis. Whether the proactivator activity of blood platelets is to be attributed to an intrinsic or adsorbed platelet component cannot be stated with certainty at present. In any event, ten-fold washing of blood platelets does not extinguish its effect.

These observations were confirmed in relation to fibrinogenolysis by determination of the so-called antithrombin VI activity[7], arising in a system composed of bovine fibrinogen, streptokinase and blood platelets. It was established that the apparent amount of antithrombin VI was directly proportional to the concentration of blood platelets present in the test system.

It seems highly probable that the proactivator activity of human blood platelets plays an important part in the spontaneous fibrinolytic activity of human blood. Indeed, the latter is known to be chiefly caused by an activator of plasminogen, probably formed by activation of proactivator[8].

RUDOLF HOLEMANS*
RUDOLF GROSS

Department of Medicine,
University of Marburg/Lahn,
West Germany.

* On leave of absence from the Department of Medicine, University of Louvain, Belgium, with a scholarship of the Deutscher Akademischer Austauschdienst.

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Precipitating Factor for Aggregated γ-Globulins in Normal Human Sera

SERA of patients with rheumatoid arthritis often form a precipitate when mixed with aggregated γ-globulins[1]. The precipitate consists of a 19 *S* γ-globulin ('rheumatoid factor'), variable amounts of 7 *S* γ-globulin and more rapidly sedimenting aggregates of γ-globulin[2]. The latter are known to be anti-complementary[3]. While studying a test for rheumatoid arthritis[4], it was found that normal human sera also form a precipitate with aggregated γ-globulins, although more slowly and less abundantly.

Aggregated γ-globulins were prepared by treating 1 per cent solutions of Cohn's human fraction II in 1/15 molar phosphate buffer, *p*H 7, containing 1 : 10,000 merthiolate, with 0·25 per cent formalin for two weeks at room temperature, followed by dialysis in the cold against the same buffer without formalin. This resulted in marked opalescence of the solutions. Ultracentrifugal analysis showed the presence of large aggregates. When mixed in capillary tubes with an approximately equal amount of human serum, these preparations yielded a precipitate after incubation for 2 hr. at 37° C. and for 18 hr. at 4° C. Sera of 200 patients, aged 5–80, with various diseases, and of 80 adolescent and adult healthy subjects, were found to react. Exceptions were found only in the sera of the 10 new-born babies tested, which showed no, or minimal, precipitate, although their mothers' sera formed a heavy precipitate.

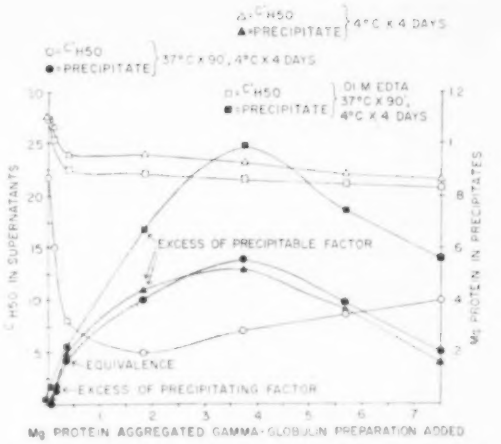

Fig. 1. Precipitating reaction between equal aliquots of normal human serum (1 ml.) and increasing amounts of aggregated γ-globulins: determination of precipitate protein, and of hæmolytic complement titre in the supernatants

Quantitative tests showed that the precipitation reaction could be inhibited by an excess of aggregated γ-globulins (Fig. 1). The supernatants were tested for presence of the precipitating serum factor (by mixing them with aggregated γ-globulins) and for the precipitable factor of aggregated γ-globulins (by mixing them with normal human serum). Three zones were thus found, one with excess precipitating factor, another with neither precipitating nor precipitable factor (equivalence), and a third with only precipitable factor in the supernatants. The amount of precipitate continued to increase beyond the equivalence zone, as is also observed in the precipitation reaction between rheumatoid serum and aggregated γ-globulins[5], as well as in classical antigen–antibody reactions, when the antigen is aggregated[6]. The amount of precipitate recovered from each tube usually failed to exceed the amount of aggregated γ-globulins added to the serum, which suggests that only a fraction of the preparation added takes part in the formation of the precipitate.

Decomplementation of the serum by absorption with 1·2 mgm. of heterologous antigen–antibody precipitates (bovine serum albumin–rabbit anti-bovine serum albumin, or egg albumin–rabbit anti-egg albumin) per ml. of serum prevented subsequent precipitation with aggregated γ-globulins.

Conversely (Fig. 1), the supernatants obtained after incubation for 90 min. at 37° C. and for 4 days at 4° C. showed a decrease in the titre of complement as measured in 50 per cent hæmolytic units. This 'anti-complementary' effect increased with increasing amounts of aggregated γ-globulins up to the area of maximal precipitation. It then, paradoxically, decreased, despite the addition of more 'anti-complementary' material, thus mirroring the decrease of precipitate. When the precipitating reaction was carried out completely at 4° C., the anti-complementary effect was much decreased (Fig. 1) and failed to mirror the amount of precipitate, which remained unchanged. This suggested a marked

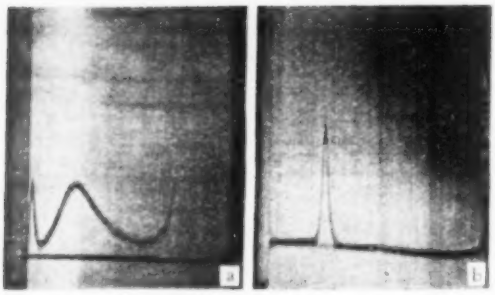

Fig. 2. Ultracentrifugal patterns of: (*a*) redissolved precipitate showing rapidly sedimenting aggregates and a small 10·5 *S* peak. Photograph taken during acceleration to 52,640 r.p.m. (*b*) purified 10·5-*S* precipitating component after removal of aggregates. Photograph taken after 32 min. at 52,640 r.p.m.

dependence on temperature for at least one step in the 'anti-complementary' effect of aggregated γ-globulins.

Fractional inactivation of components of complement[7] revealed that heat-inactivated serum (56° C. for 20 min.) deficient in the first and second components of complement, and the supernatant of serum dialysed against 0·02 molar phosphate buffer, *p*H 5·4 ('end-piece'), deficient in the first component of complement, failed to form a precipitate with aggregated γ-globulins. The redissolved precipitate ('mid-piece'), deficient in the second component of complement, formed a precipitate with aggregated γ-globulins, although 20–40 per cent less than untreated serum, and zymosan-inactivated serum, deficient in the third component of complement, and hydrazine-inactivated serum, deficient in the fourth component of complement, formed a precipitate with aggregated γ-globulins, with little or no loss of activity. These results suggested the possible identity of the precipitating factor for aggregated γ-globulins and the first component of complement. Since fixation of the latter is known to require calcium ions and to be inhibited by the chelating agent ethylenediamine tetraacetic acid[8], quantitative precipitation reactions were carried out with serum containing 0·01 *M* ethylenediamine tetraacetic acid (Fig. 1). The amount of precipitate was thereby increased, while the anti-complementary effect, measured in 50 per cent units after addition of a slight excess of calcium and magnesium ions to the supernatants, was much decreased, but not completely inhibited. These findings indicate that the precipitating factor, although suggestively similar to the first component of complement, is distinct from it as well as from the other hitherto known components of complement.

The precipitates were soluble in excess aggregated γ-globulins and in glycine buffer, *p*H 3. Ultracentrifugal examination of the acid solutions (Fig. 2) revealed a major component with an *s* rate of 9·5–10·5 *S*, large amounts of rapidly sedimenting aggregates, and frequently small 7 *S* and 19 *S* peaks. Following the removal of the aggregates by centrifugation, the major component had an $S^0_{20,\,0\cdot15\ M}$ sodium chloride of 10·5 *S* and could again form a precipitate with aggregated γ-globulins. Similar findings have been reported independently recently by Müller-Eberhard and Kunkel[9].

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A. Taranta
H. S. Weiss
E. C. Franklin

Irvington House,
Irvington-on-Hudson, N.Y.,
and
Department of Medicine and Rheumatic Diseases
Study Group,
New York University School of Medicine,
New York, N.Y.

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BIOLOGY

Five Less-Common *Salmonella* Serotypes from Congo Reptiles

During work on dried specimens of cloacal contents collected in the Parc National de la Garamba, north-eastern Congo, from various reptiles, the following serotypes of *Salmonella* were isolated: *champaign* (39 : k : 1,5) from a snake; *Crotaphopeltis hotamboeia*; *plymouth* (46 : d : 1,6) from the same specimen of snake and from a lizard, *Mabuya* sp.; *ramat-gan* (30 : k : 1,5) from the same snake specimen; *tel-aviv* (28 : y : enz$_{15}$) from a different specimen of the same species of snake; and *gatow* (6,7 : y : 1,7) from a snake *Psammophis subtaeniatus sudanensis*. The identifications were made by the Enteric Laboratory, State of Illinois, Department of Health, and confirmed by the Enteric Laboratory, Communicable Disease Center, Chamblee, Georgia.

This is the second known report of the occurrence of serotype *ramat-gan*, the first isolations having been from snakes in Israel[1]. Likewise this is the second known occurrence of serotype *gatow*, which was first isolated from the sewage of Berlin-Gatow by Hofmann and is not yet formally published although confirmed by Kauffmann[2]. The *champaign* serotype, first described from chicks by Edwards in 1945, has been reported no more than ten times, from fowl, man, diarrhœa of infants, and a bird in a zoo, and from such widely separated places as the United States, Australia and Ceylon. Serotype *plymouth* has so far been published only in a list of new serotypes issued by Kauffmann[3]. There are only a half-dozen references to serotype *tel-aviv*, three of these being from Israel, where it was twice found in chicks and later once in man. It has been reported from West Germany, France and the United States. In addition to cultures from man and chick, this type has been isolated from dog faeces, bone meal and diarrhœa of children.

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The specimens of cloacal contents were collected by soaking sterile disks of filter paper (Schleicher and Schull No. 740-*E*) and enclosing each disk in a 'Cellophane' coin envelope. On arrival by air mail in Chicago, the disks were transferred to 10-ml. brain heart infusion, incubated at 30° C., and plated at intervals on deoxycholate agar in plates of 150 mm. diameter. From each plate about 30 well-isolated colonies were picked at random for identification. Of 587 strains classified biochemically, 267 were *Salmonella*.

In general, the biochemical reactions obtained were those typical of *Salmonella*. The few exceptions are noteworthy. All 15 cultures of serotype *champaign* were indole-positive although the other reactions were typical. All but a few of 83 cultures of *gatow* gave a weak but unmistakably positive indole test in 1 per cent tryptone broth cultures 48 hr. old, using the Kovacs test. A few *gatow* cultures were negative to lysis by *Salmonella* O-phage I [4]. A few of the many *plymouth* colonies tested gave positive tests for action on gelatin, and a few others were negative with O-phage I. Some *tel-aviv* cultures were also not lysed by that phage, but all the *champaign* cultures were sensitive, as were the cultures of *ramat-gan*. Several cultures of *tel-aviv* were salicin-positive and one was positive in both salicin and sucrose. During serotyping, it was observed that a number of strains of *plymouth*, *gatow* and *tel-aviv* were monophasic and required growth in homologous phase serum broth before the alternate phase could be demonstrated.

Most of the *Salmonella* types were represented by considerable collections. Picking 30 colonies from each plate produced duplicate isolations that would not occur by the usual method of picking single representative colonies of every kind seen. Further replication occurred because the same broth culture was plated several times after different incubation periods. With the single exception of the indole reaction of *champaign*, the majority of the strains of any serotype showed typical *Salmonella* characteristics. If only a single colony had been picked, then only the atypical reactions might have been observed and a conclusion drawn that reptilian *Salmonella* exhibited atypical characteristics. In describing new serotypes on the basis of single colonies, errors may thus creep into the description. It would seem advisable to follow the zoologists, particularly the entomologists, who emphasize the need to describe new species on the basis of suitable collections rather than single specimens, so that variations can be assessed.

The extent of distribution of *Salmonella* among reptiles is remarkable. In the present work *Salmonella* were recovered from two of three snakes of one species of *Crotaphopeltis*, one of *Psammophis*, and from a lizard, *Mabuya*. They were not recovered from single specimens of *Natriciteres* and *Philothamnus*. *Salmonella* have been isolated from snakes of the latter genus by LeMinor, Ravisse and Drean[5], who also found *Salmonella* in *Crotaphopeltis*. In their series of 575 snakes from Ethiopia, Eritrea and Lybia, Serie and LeMinor[6] found no *Salmonella* in snakes of the genus *Nahia*, but did find them in various snakes of the families Colubridae and Viperidae.

The investigation of which the present observations are a part is being made to explore the question: What is the bacterial flora of reptiles, and what is the significance of the presence of *Salmonella*? The extensive literature already shows that reptiles harbour *Salmonella*. Are these part of the natural intestinal flora of reptiles, or are they acquired through association with rodents, man or other sources? The herpetologist who collected the specimens and identified the reptiles felt certain that the chance of infection from man was negligible in the area of the Parc National de la Garamba, and that the specimens came from animals which would be extremely unlikely to feed on rodents. The present work is therefore believed to suggest that *Salmonella* are naturally present in the reptilian intestine, possibly as essentially harmless commensals.

For the opportunity to examine this material, grateful acknowledgment is made to the authorities of the Parc National de la Garamba (director, Dr. V. Van Straelen), Brussels, Belgium. The specimens were collected by Dr. R. F. Inger, curator of amphibians and reptiles, Chicago Natural History Museum, who also identified the reptiles. The work was supported in part by a grant (*E*-2437) from the National Institutes of Health, U.S.A.

MacDonald Fulton
Philomena Szafran
Matthew M. Lesko

Loyola University,
706 South Wolcott Avenue,
Chicago 12.

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Use of Polyethylene Glycol in Biology

In a recent paper, I. Mackenzie Lamb[1] directed attention to the use of polyethylene glycol ('Carbowax') for the permanent preservation of algal material for microscopic study. He shows that it is practicable to preserve algae in the dry state embedded in polyethylene glycol and mounted on cards. When a portion is required for study, part of the card is snipped off and soaked in water. The alga then resumes its original state sufficiently well for detailed microscopic examination.

It seemed that such a technique could be expanded with advantage into a much wider field, and accordingly some simple experiments were carried out on plankton preserved in formalin in Aberdeen. Mixed phytoplankton, and individual copepods, decapod larvæ, chætognaths, medusæ and ctenophores were used. Phytoplankton from a preserved sample was added to a drop of 30 per cent polyethylene glycol on a slide and put aside to dry. The individual zooplankton organisms were similarly treated on slides, in a watch glass or evaporating dish according to size. Some were flooded with water the next day, others left for periods varying from a week to three months. Recovery takes only seconds on the slides, and a few minutes for the larger forms.

The phytoplankton samples were all in excellent condition and there was no difficulty at all in identifying the various species, including the delicate invertebrate larvæ, etc. The texture as seen with an oil immersion lens was surprisingly good. The chætognaths also recovered extremely well; the fin-rays, cellular structure of the corona and other features could be determined just as easily as in the originals,

and there was no difficulty at all in dissecting out the teeth. Copepods and decapod larvæ also recovered well, perhaps somewhat shrivelled but not seriously so, and certainly well enough for easy dissection of the appendages. Medusæ and ctenophores did not recover their original size and shape and remained very shrivelled, but the texture of the tentacles of the medusæ and the combs of the ctenophores remained good and identification would be possible.

Such experiments are extremely crude and should be repeated in greater detail and with a wider range of species, but the method has such attractive possibilities that it is worth bringing it now to the notice of as many workers as possible.

A 30 per cent solution of polyethylene glycol is an excellent medium in which to examine and dissect specimens under a microscope. It penetrates quickly and clears the organism to what, in my opinion, is the ideal state for handling, leaving the fine setæ still visible. It is easy to lift the dissected parts through the surface film with a needle for further examination.

In addition to Lamb's technique for the dry storage of algæ on cards, the following uses of polyethylene glycol are envisaged.

(1) Specimens of those types that recover well can be sent dry by post without special packing, and with a much-reduced risk of loss due to breakage of the jar or other container, and no risk of damage by leaking formalin to other goods in the post. Delicate or intricate specimens can be sent in a block of polyethylene glycol with no risk of displacement of parts.

(2) Micro-specimens can be sent dry, on a slide, to be recovered at the destination in such a form that they can be handled or examined by any desired technique.

(3) Parts of specimens dissected in a 30 per cent solution cannot come to harm by drying in transfer to the slide from a needle point, nor will they, or the specimen, be harmed if the observer has to leave his work to attend to something unexpected and of immediate priority. If this should result in his being unable to return to the work until after it has dried up, there is then no difficulty in resuming.

(4) Even carefully sealed museum tubes are liable to dry if not examined at regular intervals, and a minute crack, unseen at the time, can result in the complete loss of the specimen for most purposes. If preserved with polyethylene glycol added, there is a good chance that the loss would not be so serious, and a little more polyethylene glycol than the equivalent volume of the specimen simply added to the preservative should be a worth-while insurance.

It is also known as 'Carbowax' and is available in various melting points; Lamb suggests that that known as 'Carbowax 4000', melting point 55° C., is the most suitable. It is a white, rather waxy substance which dissolves readily in water, formalin and 70 per cent alcohol (but not in absolute alcohol). Specimens can be transferred to a solution at room temperature and allowed to dry if desired. For embedding in blocks, they can be transferred direct to the melted polyethylene glycol in a bath at 55° C. In Britain the cost is about 16*s.* per kgm., so that it is not expensive for so versatile and useful a commodity.

J. H. Fraser

Marine Laboratory,
Aberdeen.

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β-Glycosidase Activity and Cyanogenesis in the Susceptibility of Alfalfa to Winter Crown Rot

Hydrogen cyanide was demonstrated by Lebeau and Dickson[1,2] in alfalfa crown buds infected with an unidentified basidiomycete. They showed that a close association existed between the presence of hydrogen cyanide and mycelium in the infected buds, but did not determine whether the cyanide was produced by the fungus or host or was due to an interaction between the two. The experiments reported here were designed to clarify this problem.

Preliminary experiments were carried out to determine β-glycosidase activity of a crude enzyme preparation of the fungus cultured on a synthetic medium. Glycosidase activity of a crude enzyme preparation, obtained as the supernatant from centrifuged (13,000*g*) seven-day-old shake cultures, was determined by a modification of the Conway diffusion method[3]. 2 ml. of the crude enzyme and 1 ml. of a 0·02 *M* amygdalin solution were placed in the outer chamber and 1 ml. of alkaline sodium picrate[4] in the centre well of a Conway unit. Release of cyanide was indicated by a red coloration of the sodium picrate, which reached a maximum in 30 min. Activity of the crude enzyme preparation was not affected by dialysing but was destroyed by boiling.

Hydrogen cyanide has been reported from species of *Medicago*[5], and therefore a series of experiments was carried out to determine the effect of the crude enzyme on filtrates of *Medicago sativa* and *M. falcata*. Alfalfa crown buds obtained from plants under snow cover were homogenized for 30 min. in a Waring blender with sufficient distilled water added to facilitate homogenation. The homogenate was filtered through a double layer of cheese-cloth and the filtrate divided into two equal aliquots. Each aliquot was made up to 200 ml. with distilled water and transferred to a 500-ml. suction flask. Approximately 100 ml. of crude enzyme was added to the filtrate in one flask and an equal volume of distilled water to the other. Air was drawn through the reaction mixtures, passed through absorbent cotton and bubbled through 20 ml. of alkaline sodium picrate to indicate hydrogen cyanide production. Aeration was carried out at 15° C. for 48 hr. Control flasks containing distilled water or the crude enzyme were similarly treated. The optical densities of the picrate solutions were determined at 480 mμ using a Bausch and Lomb colorimeter. The results are shown in Fig. 1.

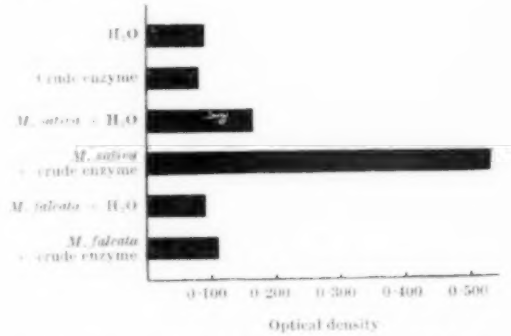

Fig. 1. Hydrogen cyanide production from filtrates of tissue homogenates of *Medicago sativa* and *M. falcata*

Hydrogen cyanide was released in an appreciable amount only from the *M. sativa* filtrate. Lack of activity with the *M. falcata* filtrate suggests that this material may have a lower glycoside content or, alternatively, contains a β-glycosidase inhibitor or a detoxification mechanism for cyanide. It appears likely therefore that production of hydrogen cyanide in infected alfalfa plants in the field is due to β-glycosidase activity on the part of the fungus and the provision of cyanogenic substrates by the host. The difference in response of the two filtrates is of particular interest since *M. falcata* is comparatively resistant to winter crown rot in the field.

Further work is being carried out, and detailed results will be reported in due course.

N. Colotelo
E. W. B. Ward

Plant Pathology Laboratory,
Research Branch,
Canada Department of Agriculture,
Edmonton, Alberta.

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Ethylene Production by Cytoplasmic Particles from Apple and Tomato Fruits in the Presence of Thiomalic and Thioglycolic Acid

Despite several tracer studies[1,2] and the use of very sensitive techniques for the detection of ethylene[3,4], there has been no clear indication of a biosynthetic pathway that can evolve ethylene in fruits. Spencer[5] reported ethylene production by cytoplasmic particles from tomato fruit in the presence of malate and co-factors. This suggested that the biosynthesis of ethylene could be related to the metabolism of organic acids in the cells. Tracer experiments by Burg[3], however, showed no evidence linking ethylene evolution to Krebs cycle metabolism. Meigh *et al.*[4] could not detect ethylene in incubation mixtures containing apple mitochondria, malate and co-factors. The latter experiments are especially significant since they used apple mitochondria known to metabolize Krebs-cycle substrates, and the system for detecting ethylene was considerably more sensitive than that used in any of the other investigations. It therefore appears that ethylene synthesis in fruits must be associated with some other aspect of organic acid metabolism.

Recently we have isolated cytoplasmic particles, from apples and tomato fruits, that evolve ethylene in the presence of thiomalic and thioglycolic acid. Cysteine, glutathione, methionine, and other related compounds (thiodiglycolic acid, α-monothioglycerol, β-mercaptopropionic acid, carboxymethylmercaptosuccinic acid) did not replace the requirement for thiomalic or thioglycolic acid. Results of a number of experiments with particles from apples are summarized in Table 1. Similar results were obtained with particles from tomato fruit.

These ethylene-producing systems have many characteristics of an enzymatic process. The rate of ethylene production is proportional to the concentration of the particles. The rate, during a 45-min. period, is approximately proportional to the length of the incubation, and the reaction is essentially inhibited by heat denaturation. The reaction appears to be stimulated considerably by phosphate. Furthermore, some chelating agents that inhibit enzymatic reactions, such as diethyldithiocarbamate (DIECA) and ethylenediamine tetraacetic acid (EDTA), markedly inhibited this reaction and the inhibition is partially reversed by the addition of copper to the system.

Table 1. Ethylene Production by Cytoplasmic Particles from Apples in the Presence of Thiomalic and Thioglycolic Acid

Flask content*			Ethylene† (μl./mgm. N/hr.)
Thiomalic	+ co-factors	+ no particles	0·0
Thioglycolic	+ ,,	+ no particles	0·0
Thiomalic	+ ,,	+ particles	0·019
Thioglycolic	+ ,,	+ particles	0·016
Thiomalic	+ ,,	+ denatured particles	0·0004
Thiomalic	+ ,,	— PO_4 + particles	0·004
Thiomalic	+ ,,	+ DIECA + particles	0·003
Thiomalic	+ ,,	+ DIECA + 10^{-5} *M* copper sulphate + particles	0·006

* The flask contents consisted of the following: 50 μm. thiomalic or thioglycolic acid, 3 μm. adenosine triphosphate, 60 μm. phosphate, 0·08 μm. coenzyme-A, and 400 μm. sucrose. 1 ml. of particulate suspension containing approximately 1·5 mgm. nitrogen was added to each flask. The flasks were incubated 2 hr. at 30° C. in an automatic shaker. The pH of the reaction mixture was 6·2.

† Ethylene was determined by gas chromatography with a system previously described (ref. 4). The method was sensitive to 3×10^{-5} μl. of ethylene in a 1-ml. sample.

It is noteworthy that these preparations did not oxidize Krebs cycle substrates. Another important difference between mitochondria and these particles is in the pH of the isolating media. Whereas active mitochondrial particles are isolated from homogenates of neutral or slightly alkaline media, it was found necessary to isolate these particles from homogenates of acid media. Particles that cause the evolution of ethylene were obtained from fractions precipitated at 500*g*, 16,000*g* and 40,000*g*.

These findings offer a completely new approach to the study of ethylene biosynthesis. Work is now in progress on the purification of the enzyme or enzymes and the elucidation of the mechanism of the reaction by tracer techniques.

M. Lieberman
C. C. Craft

Pioneering Research Laboratory for
Post-Harvest Physiology,
Market Quality Research Division,
Agricultural Marketing Service,
U.S. Department of Agriculture,
Plant Industry Station,
Beltsville, Maryland.

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ENTOMOLOGY

Ribonucleic Acids in the Moult Cycle of an Insect

It is well known that the cuticle in insects is shed at the end of each instar and a new one is formed by the underlying epithelium. Although much is known about the histological changes in the epithelium and the chemical changes in the cuticle during this complicated process of moulting[1,2], nothing is known about the role of the ribonucleic acids (RNA) during

this period. Since it is known that RNA plays an important part in cellular protein synthesis[3], it was considered desirable to study the RNA of the insects during the moult cycle.

In the present investigation the nymphs of *Gryllus bimaculatus* were used. Young nymphs, hatched within a period of 15 hr., were separated and maintained in the laboratory under identical conditions of temperature, light, humidity, etc., so that their rate of growth would be the same. Prior to the extraction of RNA, the nymphs were homogenized and treated successively with 2 per cent perchloric acid and an alcohol–ether mixture in order to remove the nucleotides and the lipids respectively. RNA was extracted by treating the residue, in the cold, with *N* perchloric acid for 18–24 hr. and estimated by the ultra-violet absorption and/or the orcinol method in the presence of ferric chloride. For purposes of comparison, total nucleic acids were extracted with warm 0·5 *N* perchloric acid and RNA was estimated by the orcinol reaction[4]. Histological preparations of nymphs fixed in Zenker's fluid have also been made and were stained with Unna's methyl green–pyronin stain.

The first-stage nymphs of *Gryllus bimaculatus* moult approximately at the end of the fifth day after hatching, while those of the second stage moult, usually, on the sixth or seventh day after the first moult. There is considerable individual variation in the time taken by the nymphs in the succeeding stages. Hence, for the quantitative estimations of the RNA, only individuals of the first two stages were used during this work.

Results are given in Table 1.

Table 1

Age of the nymph after hatching or moulting (days)	RNA content per mgm. weight of nymph (µgm.)	Total RNA per individual (µgm.)
1	7·2	5·6
2	5·1	4·6
3	4·5	8·1
4	0·7	1·3
5	0·7	1·3
Soon after first moult	0·8	1·6
1	2·1	6·3
2	2·4	7·5
3	5·4	21·2
4	7·6	32·0
5	2·4	11·0
6	0·7	3·3
Second moult		

It can be seen from Table 1 that the RNA content per mgm. wet weight of the nymph gradually falls from the time of hatching to the first moult, and then rises to a peak at the intermoult period; it decreases once again to a minimum at the time of the second moult. However, if we consider the total ribonucleic acid content per individual, it is evident that the RNA content reaches its highest figure, both in the first- as well as in the second-moult stage nymphs, at the middle intermoult period, that is, before the nymph is actually preparing for the succeeding moult. There is thus a gradual accumulation of RNA until the nymphs are preparing for the moult, and a sudden fall during the pre-moult period.

The histological preparations stained with Unna, after treatment with ribonuclease, or with buffer or without any pretreatment, showed a similar fluctuation in the ribonucleic acid content as indicated by the intensity of staining. The nucleoli in the chitogenous epithelium, which are prominent by their strong pyroninophily in the intermoult period (Fig. 1) are less visible in nymphs preparing to moult and in those which have just emerged from the moult (Fig. 2). Staining of the newly moulted (early post-moult stage) nymphs of the first five stages also showed faint staining of the nucleoli when compared with those of the intermoult stage nymphs. As the range of individual variation in the time taken for moult from the third stage onwards is great, day-to-day observations were no longer useful. However, such observations of the first two stages suggest that the nucleoli gradually become more prominent after the moult until the onset of the succeeding moult. On the contrary, the cytoplasm of the epithelial cells shows greater avidity for pyronine when the new cuticle is being laid, that is, just before and soon after the moult; while in the intermoult period, it is less pyroninophilic. In the adult insects of varying ages the epithelium shows only faint staining with pyronine both in the nucleoli and the cytoplasm.

Fig. 1. Chitogenous epithelium of an intermoult second-stage nymph stained with Unna

The results reported above suggest that there is a gradual accumulation of RNA in the nymph from the time of moult until the late-intermoult period, and then a sudden decrease. Observations with methyl green pyronin further show that the basophilia of the nucleolus and of the cytoplasm undergoes cyclic changes during the moult cycle, suggesting that nucleolar RNA might be transferred to the cytoplasm at the pre-moult stage. Finally, these observations indicate that the hormone which is secreted by the prothoracic glands and which is known to reach a titre sufficient to cause moulting some time before the processes involved in moulting are actually initiated[5,6] might influence the release of nucleolar RNA into the cytoplasm.

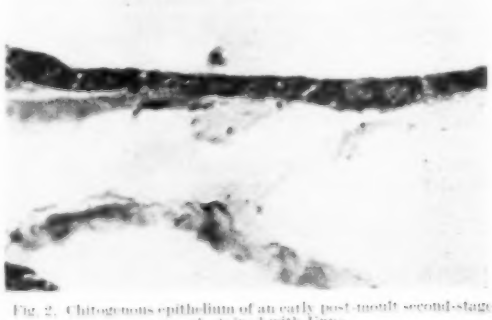

Fig. 2. Chitogenous epithelium of an early post-moult second-stage nymph stained with Unna

I thank Prof. J. Brachet for guidance, encouragement and facilities.

A. KRISHNAKUMARAN*

Laboratoire de Morphologie animale,
Université libre de Bruxelles,
Bruxelles.

* Permanent address: Department of Zoology, Sri Venkateswara University, Tirupati, A.P., India.

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Trans-2-Hexenal in the Scent Gland of the Hemipteran *Acanthocephala femorata*

THE plant bug, *Acanthocephala femorata* (Fab.), is one of the many hemipterous insects which eject odoriferous materials when disturbed. This large brown coreid, which occurs in the southern United States, is frequently found on citrus plants[1].

The scent gland secretion of *Acanthocephala* adults is stored in a large round reddish-orange sac which lies on the floor of the body cavity covering the metathoracic and first abdominal segments and extending to the second abdominal segment. This sac opens to the outside of the body-cavity through a pair of ostioles each of which is located on a suture between the sternal plate and the pleural plate of the metathorax. The ducts leading from the sac to the ostioles enlarge just inside each ostiole and can be opened to the outside by means of muscle-operated lips. The sac itself contains no obvious musculature for compression which would be required for ejection of the secretion. However, it was observed that ejection always occurred when the metathoracic legs were flexed. If the metathoracic legs were held immobile, no ejection occurred. Indeed, it was observed that movement of metathoracic coxae from which the femora had been severed was coincident with ejection of the secretion. It is possible that the force required for ejection of the secretion is supplied by coxal pressure during contraction of the metathoracic leg; the secretion thus would be ejected when the lips of the sac ducts are simultaneously opened.

The secretion of *Acanthocephala* adults and nymphs issues as fine droplets. The adult secretion can be sprayed for a distance of at least 8 in. If one side of the body is mechanically stimulated, the spray is unilateral from the stimulated side. However, if the dorsum of *Acanthocephala* is stimulated, the spray is often bilateral.

Samples of clear yellow fluid from the sac were obtained by removing the abdominal dorsum and viscera of *Acanthocephala* and piercing the exposed sac with a fine capillary. Fluid collected in capillaries was identified as *trans*-2-hexenal by infra-red spectrophotometry, mass spectroscopy and the 2,4-dinitrophenylhydrazone derivative.

For infra-red spectrophotometry, a film of the secretion was used. The resulting spectrum demonstrated that the *Acanthocephala* secretion was a conjugated aliphatic aldehyde exhibiting *trans* deformation. The absorption bands were: aldehyde C—H, 3·66μ; C=O, 5·89μ; C=C, 6·08μ; *trans* C=C, 10·25μ. The spectrum was identical to that of 2-hexenal[2].

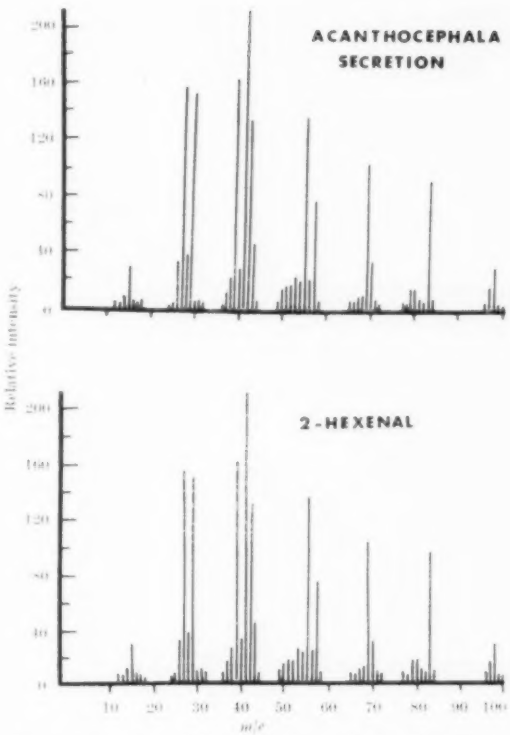

Fig. 1. Comparison of the mass spectra of 2-hexenal and the *Acanthocephala* secretion

The compound was analysed in a modified Consolidated 21-102 analytic mass spectrometer by injecting the compound with a microsyringe into the heated inlet system (100° C.) of the instrument. A normal magnet run at a pressure of 65·22μ indicated no masses above 98. A high magnet run further established the absence of any higher boiling components. Analysis of the structural fragmentation pattern established the *Acanthocephala* secretion as a hexenal which was identical with that of synthetic 2-hexenal (Fig. 1). Virtually superimposable fragmentation patterns indicated that the *Acanthocephala* secretion was a pure enal.

The 2,4-dinitrophenylhydrazone of the enal was prepared by adding an alcohol solution of the secretion to a saturated solution of the reagent in 2 *N* hydrochloric acid. The purified derivative melted at 144-145° C. uncorrected and did not produce a melting point depression in admixture with the derivative of synthetic 2-hexenal melting at 145-146° C.[3]. The elementary analysis of the *Acanthocephala* derivative corresponded to hexenal (found: C, 51·52; H, 5·15; N, 19·89; calculated for $C_{12}H_{14}N_4O_4$: C, 51·79; H, 5·04; N, 20·14 per cent).

2-Hexenal has also been found in the cockroach *Eurycotis floridana*[3]. In this insect the secretion is stored in a sac which opens to the outside of the body between the sixth and seventh abdominal sternites. It is of interest to note that males of the giant water bug *Lethocerus indicus* (Lepeletier and Serville) produce the acetate ester of 2-hexenal, which is given

off through tubules located in the abdomen[4]. Elsewhere, 2-hexenal has been found in whale oil[5] and is a common constituent of plants[6].

Nothing is known of the function of 2-hexenal in Nature. It may serve as a repellent for predators of *Acanthocephala*. In the laboratory, *Acanthocephala* sometimes ejected this compound at imported fire-ants (*Solenopsis saevissima* var. *richteri* Forel) which were approaching. The ejection was unilateral to the side facing the ants and caused the ants to move away. When the ants actually attacked *Acanthocephala* it always ejected copious quantities of the secretion.

We are indebted to Dr. R. P. Curry of the Ethyl Corporation, Baton Rouge, Louisiana, for helpful discussion of the infra-red spectra and Prof. P. S. Callahan of Louisiana State University for morphological interpretations.

Murray S. Blum
Ronald D. Crain*
Julius B. Chidester*

Department of Entomology,
Louisiana State University,
Baton Rouge, Louisiana.

* Ethyl Corporation, Baton Rouge, Louisiana.

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BACTERIOLOGY

Hæmolytic Activity of *Corynebacterium ovis*

The Preisz–Nocard bacillus (*C. ovis*) which is responsible for a number of diseases of animals, including caseous lymphadenitis of sheep and ulcerative lymphangitis of horses, grows well on blood-agar medium, producing circular, opaque surface colonies which are frequently surrounded by a narrow zone of hæmolysis.

The hæmolysin, which is active against guinea pig, rabbit, horse and sheep corpuscles, is thermostable, non-antigenic and appears to be closely linked to the bacterial cells so that it cannot be obtained free in a filtrate[1].

During an investigation of the effects on animal erythrocytes of combinations of diffusible substances produced by bacteria (to be published), it was observed that mixed cultures of *C. ovis* and *C. equi* showed a synergistic hæmolytic effect on sheep, goat, ox and rabbit cells. The phenomenon was better illustrated by streaking the strains at right angles to each other on the surface of 1·5 per cent nutrient agar plates containing 4 per cent red cells which were previously washed three times in normal saline and re-suspended to the original volume of the blood. The inoculated plates were incubated in air-tight jars in a mixture of 10 per cent carbon dioxide and 90 per cent air, at 37° C. for 24–48 hr.

Fig. 1 shows the effect on sheep blood agar after 48-hr. incubation with the vertical culture streak of *C. ovis* running through the horizontal streak of *C. equi*. The hæmolytic pattern obtained is the result of the interaction of the diffusible products of both

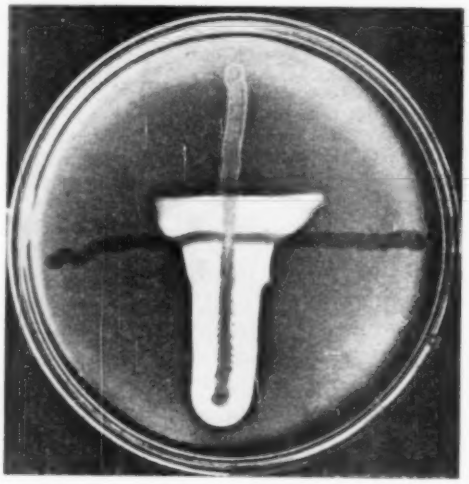

Fig. 1. Sheep blood-agar plate showing the hæmolytic effect of *C. ovis* in the presence of *C. equi*

strains; that of *C. ovis* being active over a larger area than *C. equi* and neither exerting the hæmolytic effect independently. Unlike the hæmolysin described by Carne, the diffusible substance produced by *C. ovis* is active against ruminant and rabbit cells, but not horse red cells, and its effect is enhanced by the presence of 10 per cent carbon dioxide.

The plate method, which appears to be more sensitive than tube titration, has also been used to show that the diffusible product of *C. ovis* is filtrable and is capable of dialysation through 'Cellophane'; and is being adapted for antigenic studies.

These preliminary observations suggest that an indicator system of animal erythrocytes previously treated with an actively growing culture of *C. equi* may prove of value in elucidating the true nature of the hæmolysins of *C. ovis*.

Gordon Fraser

Department of Veterinary Bacteriology,
Royal (Dick) School of Veterinary Studies,
University of Edinburgh.

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Inhibition of Multiplication of Bacteriophage by Actinomycin

It has recently been found that actinomycin forms a complex with deoxyribonucleic acid but not with ribonucleic acid[1]. In this communication we wish to present evidence to show that the antibiotic prevents multiplication of the phage while permitting the growth of the host bacterium.

The actinomycin used in these experiments was crystalline actinomycin *S*[2,3], supplied by the Daiichi Seiyaku Pharmaceutical Co., Ltd. The standard methods used for handling bacteria and phage and for determining nucleic acid were those described in another communication[4].

Actinomycin *S* is known to prevent the growth of Gram-positive bacteria, but *Escherichia coli B*, a Gram-negative bacterium, used in this experiment, can grow actively in the presence of the antibiotic. Exposure of free *T2r* phage to 100 μgm./ml. of actinomycin *S* for 60 min. at 37° C. did not cause any

inactivation of the phage. The effect of the antibiotic on phage reproduction was studied. Cells of *E. coli B*, harvested during the logarithmic phase of growth, were infected with *T2r* phage and shaken at 37° C. in a glucose-salt synthetic medium with various concentrations of actinomycin *S*.

The results are illustrated in Table 1, which shows that the reproduction of *T2r* phage is progressively impaired by increasing concentrations of actinomycin *S*, while the synthesis of deoxyribonucleic acid in the phage-infected cells is not affected by the antibiotic. It must be emphasized that the infected bacteria produce deoxyribonucleic acid in a similar way even when the antibiotic is added 5 min. either before or after infection.

Table 1. Effect of Actinomycin S on the Multiplication of Phage and the Synthesis of Deoxyribonucleic Acid by *T2r*-infected Bacteria

Concentration of actinomycin S (μgm./ml.)	Relative increase (percentage of control)	
	Phage titre	Amount of deoxyribonucleic acid
0	100	100
1	45	—
3	29	—
10	12	98
30	10	94
100	4	87

The lysate obtained in the presence of a level of 30 μgm./ml. of actinomycin *S* contained nearly the same amount of the deoxyribonucleic acid as that found in the untreated control lysate, but the infectivity of the former lysate was only one-tenth of the latter. When the lysates were centrifuged at 3,000*g* for 15 min., the majority of the deoxyribonucleic acid was found in the supernatant fluid, both in the presence and in the absence of the antibiotic. Hence analyses were made on these supernatant fluids. As shown in Table 2, a significant difference between the control and the antibiotic-treated lysates was revealed by comparing the amount of deoxyribonucleic acid in the sediment obtained by centrifugation at 20,000*g*. At this gravity, normal *T2r* phage but not free nucleic acid was sedimentable. Furthermore, the deoxyribonucleic acid which had been produced by infected cells exposed to the antibiotic was not precipitable by anti-*T2r* phage serum and was sensitive to deoxyribonuclease. These results indicate that this deoxyribonucleic acid has no protein coat reacting with the antiserum and protecting the viral deoxyribonucleic acid from deoxyribonuclease.

These effects of actinomycin *S* on phage reproduction are essentially similar to those of proflavine[5]. One may suppose that actinomycin *S*, like proflavine, blocks some final step in the maturation of the phage.

Table 2. Properties of Deoxyribonucleic Acid in the Lysate made in Presence of Actinomycin *S*

Fraction	Deoxyribonucleic acid found*	
	Control lysate	Lysate with actinomycin *S*
Initial lysate	100	100
Low-speed centrifugation supernatant	90	73
Sediment at 20,000*g*	34	2
Precipitate with antiserum	53	2
Deoxyribonuclease-resistant	39	10

* Values in each fraction represent percentage of the amount of deoxyribonucleic acid in the initial lysate.

However, there is a significant difference between the action of two inhibitors; the formation of infective phage is reversed by removal of proflavine, but not by removal of actinomycin *S*. Thus further work is necessary to determine whether normal viral protein is produced by the antibiotic-treated cells.

Atsuo Nakata
Mutsuo Sekiguchi*
Junichi Kawamata

The Research Institute for
Microbial Diseases,
Osaka University,
Osaka, Japan.

* Department of Biology.

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VIROLOGY

Effect of an Organic Gold Salt on Eaton's Primary Atypical Pneumonia Agent and Other Observations

Eaton, Liu and their colleagues have provided evidence that the causative agent of a certain type of human primary atypical pneumonia, namely, that in which a proportion of patients develop serum agglutinins against *Streptococcus MG* and human erythrocytes at 4° C., is filterable, can be propagated in the lung of the chick embryo, and produces lung lesions when inoculated into hamsters and cotton rats by the intranasal route[1]. Some uncertainty exists about the nature of this organism. The strains studied had a large particle size (between 180 and 250 mμ as measured by filtration[1b]); some were sensitive to streptomycin[2] and all to tetracyclines[3].

We have observed that the macroscopic and microscopic lesions produced in the hamster lung by the intranasal inoculation of chick embryo lung infected with the 'Hetter' strain of Eaton's primary atypical pneumonia agent resemble in some respects those seen in the lungs of mice infected intranasally with cultures of pleuropneumonia-like organisms[4].

The size of Eaton's organism is of a similar order to that given for the elementary particles of some pleuropneumonia strains (125–250 mμ), and its pattern of antibiotic sensitivity is also similar to that of the pleuropneumonia group[5]. Eaton and his colleagues were unable, however, to grow pleuropneumonia-like organisms from egg material containing strains of the organism[2].

It has been shown that organic gold salts will suppress lung[6] and other lesions[7] produced by pleuropneumonia-like organisms in animals, and accordingly we have investigated the effect of sodium aurothiomalate ('Myocrysin', May and Baker) on experimental infections with Eaton's primary atypical pneumonia agent in hamsters and chick embryos. The 'Hetter' strain of Eaton's agent, obtained from Dr. C. Liu and kindly given to us by Prof. C. H. Stuart-Harris (Sheffield), was used for all the experiments and was passed by the amniotic route in 13-day-old chick embryos. Infection was recognized in frozen sections of the lungs of the chick embryos by using the indirect fluorescent antibody method with a 'middle layer' consisting either of a pool of convalescent-phase sera from local patients with primary atypical

pneumonia or, for checking, of a specific rabbit antiserum against the classical 'Mac' strain kindly provided by Dr. M. D. Eaton (Boston).

Groups of hamsters were inoculated intranasally with 0·6 ml. of a 10 per cent suspension of infected chick embryo lung. Some groups were given a daily dose of 3–5 mgm. of sodium aurothiomalate intraperitoneally. Others were kept as untreated controls or injected with the excipient without the gold salt. All groups were killed 11 or 12 days after intranasal inoculation and the intensity of their lung lesions graded on two arbitrary scales depending on (*a*) the macroscopic degree of lung consolidation, and (*b*) the proportion of bronchi and vessels with cuffs of mononuclear cells and the degree of alveolar consolidation seen in lung sections.

Table 1 shows the results obtained in experiments with four different egg passage-levels of the 'Hetter' strain. There was a consistent reduction in the intensity of the lung lesions in hamsters treated with gold. The lung lesions were also reduced to a similar degree (an average macroscopic lesion score of 0·12 was obtained as part of exp. 4) by a convalescent-phase serum from a local patient (Ev. 8) with primary atypical pneumonia. This serum had a fluorescent antibody staining titre of 1 in 50 to 1 in 100 when titrated on infected chick embryo lung sections; the patient's acute-phase serum did not stain at a dilution of 1 in 5. This neutralization provides an indirect check that the lesions produced in hamsters, and inhibited by the gold salt, were in fact caused by the 'Hetter' organism and not by a second (hypothetical) organism present in the egg material but unrelated to Eaton's agent.

Table 1. Effect of Sodium Aurothiomalate on the Lung Lesions produced in Hamsters by Eaton's Primary Atypical Pneumonia Agent

Exp. No.	Controls			Gold-treated		
	No. of animals	Average lesion score		No. of animals	Average lesion score	
		Macroscopic	Microscopic		Macroscopic	Microscopic
1	3	1·5	4·6	4	0·25	1·5
2	8	1·6	6·0	7	0·14	1·0
3	9	1·7	5·8	9	0·3	1·2
4	9	1·6	4·9	7	0·07	1·1

Analysis of the frequency distribution of the individual lesion scores for all fifty-six hamsters indicates that the differences between treated and untreated groups were unlikely to have arisen by chance alone. Macroscopic lesion scores: $\chi^2 = 31·5$; d.f. $= 5$; $P < 0·001$; microscopic lesion scores: $\chi^2 = 53·3$; d.f. $= 8$; $P < 0·001$.

In other experiments a single dose of 25 or 30 mgm. of sodium aurothiomalate was placed in the yolk sac of chick embryos either before, or at the same time as, the inoculation of a suitable dilution of the 'Hetter' seed into the amniotic cavity. Subsequent examination of frozen sections of the chick embryo lungs showed that substantially fewer of the treated groups had specific antigen ('fluor-stained antigen') when examined by the indirect fluorescent antibody method. Also pools of lung tissue from the treated embryos did not produce pneumonia in hamsters, whereas those from the control, untreated embryos did so.

These results are in accord with the view that Eaton's primary atypical pneumonia agent may be biologically related to the pleuropneumonia group. However, more information on the effect of gold on accepted viruses is required, although Bauer[8] found that neurovaccinia was not inhibited.

The results of intensified Giemsa-staining of sections of chick-embryo lung infected with the 'Hetter' strain also suggest an affinity between the agent and pleuropneumonia-like organisms. Acetone-fixed, frozen sections (about 5μ) were treated with 1 per cent potassium permanganate[9] for 2 min., washed and stained with 1 in 25 Giemsa in phosphate-buffer *p*H 6·4 for 18 hr. They were differentiated with 0·5 per cent acetic acid, washed and then either mounted in a mixture of equal parts of glycerol and phosphate-buffer and examined at once or—with more distortion and variability—dehydrated with acetone, cleared with xylol and mounted in a polystyrene (*DPX*).

Minute pink coccobacilliform bodies were seen in association with the bronchial epithelial cells. Some were intracellular, but the majority appeared to be arranged as a compact layer on the surface of the cells, and they seemed to occupy virtually the same position as the fluor-stained antigen found in adjacent or other sections of the chick-embryo lungs. (In our experience the exact location of the fluor-stained antigen is difficult to judge with the fluorescence microscope. The antigen might be completely within the cytoplasm of the bronchial epithelial cells and just under the cell membrane or, alternatively, it might be predominantly on the surface of the cells with some material taken into the cells by phagocytosis.) Coccobacilliform bodies have not yet been seen in sections of uninfected chick-embryo lungs. A close correlation has, however, been observed between the presence of fluor-stained antigen and coccobacilliform bodies in embryos inoculated with a variety of positive or negative materials. The coccobacilliform bodies appear at about the same time—three to four days after inoculation—as the fluor-stained antigen in injected chick-embryo lung, and, like the antigen, they are suppressed or reduced in quantity in embryos treated with sodium aurothiomalate. Further experiments are being carried out to obtain evidence from other directions on the identity, or otherwise, of the coccobacilliform bodies and the specific fluor-stained antigen.

As these findings may be peculiar to our sub-line of the 'Hetter' strain, it now seems desirable that other strains of Eaton's primary atypical pneumonia agent should be examined elsewhere for coccobacilliform bodies by the method of mild fixation and intensified Giemsa staining, and that they should also be tested for sensitivity to organic gold salts *in vivo*.

B. P. Marmion

Public Health Laboratory Service,
York Road, Leeds, 15.

Gillian M. Goodburn

Department of Bacteriology,
University of Leeds.

June 14.

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Hæmagglutination and Hæmagglutination-Inhibition with African Horse-Sickness Virus

COMPLEMENT-fixation and mouse neutralization tests are the two techniques so far employed in serological work with African horse-sickness virus. It was thought worth while to study the hæmagglutinating properties of this agent with the view of obtaining yet another tool for epidemiological (epizootiological) studies of this dreaded horse disease.

The three strains studied were an Indian strain recently isolated from the lung of a dead horse, a Pakistan strain and an attenuated type 6 strain from South Africa. The latter two were kindly supplied by Dr. Alexander of the Onderstepoort Laboratory in South Africa. The Indian and the Pakistan strains had undergone approximately 20 and the type 6 strain probably 100 or more mouse brain passages.

The basic techniques for preparing antigens, sera and erythrocytes for hæmagglutination-inhibition test were those described by Clarke and Casals[1]. Antigens prepared from infected suckling mouse brains were: (1) acetone–ether extract; (2) sucrose–acetone extract; (3) sucrose–acetone extract treated with protamine sulphate; (4) crude aqueous alkaline extract; (5) the same treated with protamine sulphate. Control antigens were prepared from the brains of normal healthy mice of the same age. Erythrocytes collected from roosters, geese, sheep, guinea pigs, horse, mule and donkey were tested. The cell concentrations used ranged from 0·4 per cent to 1 per cent. The cells were suspended in 'adjusting diluents', which when mixed with an equal volume of 'serum–virus diluent' gave a *p*H range from 6·4 to 7·0. The hæmagglutination test was performed in tubes with 0·5 ml. of antigen and 0·5 ml. of required cell suspension. One set was incubated at 37° C., one at room temperature (25° C.) and one at 4° C.

Initial experiments revealed that this virus showed hæmagglutination with cells from the equines alone. As the most satisfactory pattern was obtained with horse cells, these were used for all further work. Only the two antigens (Nos. 3 and 5) treated with protamine sulphate showed hæmagglutination. Of the two, sucrose–acetone extract treated with protamine sulphate gave better results than crude extract treated with protamine sulphate. Control antigens prepared from normal mouse brains in the same manner did not show any hæmagglutination. The best results were obtained with 0·5 per cent horse red blood cells, using *p*H 6·4 and incubation at 37° C. The test was read within 1½–2 hr., when the cell controls had settled. The three strains gave similar hæmagglutination titres ranging from 1 : 32 to 1 : 128.

Hæmagglutination-inhibition work is still in a preliminary stage. Removal of non-specific inhibitors from sera was attempted by treatment with kaolin, acetone extraction and inactivation at 56° C. for 30 min. Antigen and serial two-fold dilutions of serum were mixed in 0·25 ml. volumes and incubated either at 37° C. for 1 hr. or overnight at 4° C. After incubation, 0·5 ml. of cells was added. Of the three methods of treating sera, acetone extraction appeared to be the best. From the limited trials it seemed that kaolin might reduce the level of specific antibodies. Overnight incubation at 4° C. produced better results than those observed with incubation at 37° C. for 1 hr.

Table 1

Serum No.	CF titres (reciprocal of initial serum diluted with 4 units of antigen Indian strain)	Log neutralization index*	HI titres (reciprocal of initial serum diluted with 4 units of antigen Indian strain)
603360–3	32	3·1 to ≤ 3·5	40–160
603366–5	8	3·0 to ≤ 3·1	20–80
603381–4	32	2·5 to ≤ 3·7	160–640
603390–3	16	≤ 3·5	80–320
603661–2	8	2·2 to ≤ 4·0	20–80
603665–2	32	2·7 to ≤ 4·0	40–160

* Adult mouse IC test with several Indian strains, using constant serum-varying virus dilutions.
CF, Complement-fixation; HI, hæmagglutination-inhibition.

A group of horse sera collected during a recent epidemic in India were tested for hæmagglutination-inhibition. Six sera that did not show detectable complement-fixing and neutralizing antibodies were also negative for hæmagglutination-inhibiting antibodies. Table 1 compares the complement-fixation, neutralization and hæmagglutination-inhibition results of the remaining six sera. The hæmagglutination-inhibition pattern, while clearly indicating inhibition, is not yet entirely satisfactory. The end-point is not as sharply defined as in tests with other viruses but is spread over several tubes. For this reason the hæmagglutination-inhibition titres have been presented as ranging over several tubes.

McIntosh[2] has reported that the complement-fixation test is less type-specific than the neutralization test and that no antigenic differentiation between the heterotypic strains was possible. Work is in progress to determine if the hæmagglutination-inhibition test is type-specific.

I wish to thank Drs. Tara B. Gokhale and Keerti V. Shah for carrying out the complement-fixation and neutralization tests.

KHORSHED M. PAVRI

Virus Research Centre,
Poona.

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GENETICS

Developmental Barriers in a Selection Experiment

THE present experiments describe the effect of selection on expression of the *ocelli-less* mutant, sex-linked recessive, affecting the ocelli and three pairs of macrochaetes on top of the head in *Drosophila subobscura*.

In the foundation population, homozygous for the *ocelli-less* mutant, a large number of flies lacked all 3 ocelli and all 6 bristles; in the rest, varying combinations of bristles and ocelli were present. The ocelli in some of the flies were found to be slightly displaced from their normal positions, and in certain cases their sizes were also affected. In a few flies the bristles were found to be repeated; instead of one normal bristle on one side, additional bristles were found to lie close to the normal bristle. A positive correlation ($r = 0{\cdot}46$) was found between the presence of bristles and of ocelli. Therefore, in measuring the degree of expression, a unit score was given for the presence of each of the 6 bristles and 3

ocelli. Thus a fly completely lacking ocelli and bristles would have a total score of zero and a wild-type fly a total score of 9. No addition to the total score was made for repeated bristles; but their frequency was recorded in the foundation population and in the last few selected generations. The word 'score' will be used throughout in the sense here defined.

In the foundation population the mean score of females was 1·76 and of males 1·44; the sex difference, although small, was found consistently in all the cultures scored.

Directional selection was effective in increasing the mean number of ocelli and bristles almost to the wild-type score of 9 in the upward direction, and decreasing the score to zero in the downward direction. Both the variance of the score and the sex difference in score were greatest in populations the mean score of which was at the centre of the range.

The distribution of the phenotypes in the selected populations suggested that there exists a developmental barrier which prevents progress beyond the upper and lower bounds. These bounds were sharper in the downward direction because other bristles were rarely affected by the mutant. The flies, however, after reaching the score of zero, showed a notch-like depression on the lower margin of the head, which varied in the degree of expression. In the upward selected population, in the last generations of selection, a few flies with extra ocelli were seen, and the frequency of repeated bristles was found to be considerably greater than that in the foundation population.

In Fig. 1 a genetic model is shown to explain the bounded distribution of phenotypes, in terms of genes which in their primary effects on an ocelli-bristle-forming substance are additive throughout the range.

In Fig. 1*a* it is supposed that there are a number of pairs of alleles which alter the expression of the *ocelli-less* flies by altering the amount of some 'precursor' which is necessary for the formation of ocelli and bristles, and which is normally present in the required amount in wild-type flies having the $+^{oc}$ gene. In *ocelli-less* flies the amount of this precursor is variable, but usually less than in flies carrying the $+^{oc}$ gene. Now if the amount of the precursor is less than T_1, no ocelli or bristles are formed. If it is between T_2 and T_3 the wild-type score of 9 is produced. Flies having amounts of precursor intermediate between T_1 and T_2 tend to produce intermediate scores. Only flies having the amount of precursor greater than T_3 produce a score greater than 9. That flies with an amount of precursor within the range T_2–T_3 should all have the same phenotype of 9 is to be expected from Waddington's argument concerning canalization[5]. The amount of precursor in flies carrying the $+^{oc}$ gene is unlikely to be absolutely constant. If we suppose, as shown in the diagram, that $+^{oc}$ flies have an amount of precursor within the range T_2–T_3, then canalizing selection during the past evolution of the species would ensure that the same adult phenotype would develop provided that the amount of precursor is within this range.

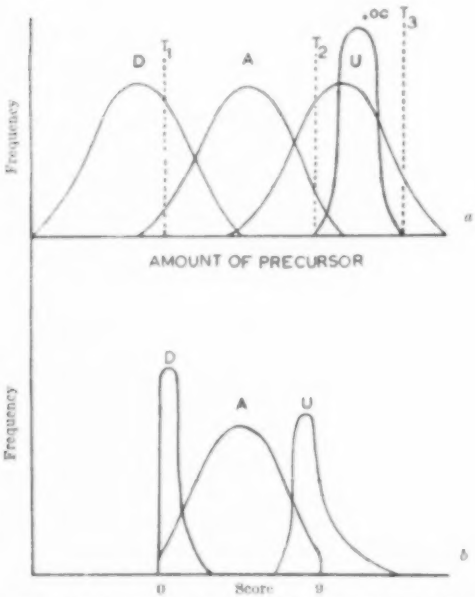

Fig. 1. Model to explain the bounded distribution of phenotypes

The three populations *A*, *D* and *U* in Fig. 1*b* represent, respectively, the phenotypes of a population with a mean score at the centre of the range and downward and upward selected populations. In *A* the genetic variance of the score is largely additive, but in populations *D* and *U* the genetic variance of the score is largely epistatic.

The concept of the 'amount of precursor' has been introduced to facilitate the discussion. A similar model could be given if it were assumed that the different scores are determined by differences in the competence of cells to respond to an unvarying pre-pattern[4].

On the basis of this model most of the experimental results can be explained satisfactorily. A similar model has been suggested by Rendel to explain the results of selection on the scute phenotype in *Drosophila*[3]. However, the situation is complicated by the fact that in some of the flies repeated bristles or bristles at new sites were seen, even in the absence of other bristles or ocelli, suggesting that the flies are abnormal not only in the amount of the precursor but also in its distribution. The main aim of the model, however, is to show how a bounded distribution of adult phenotypes with epistatic genetic variance could be the result of a character, which, if measured earlier in development, is continuously varying and of which the genetic variance is additive.

A more detailed account of this work is given elsewhere[5]. The genetic mechanisms responsible for the distribution of the ocelli-bristle-forming precursor have been described by Maynard Smith and Sondhi[1]. By selecting flies for the symmetrical and asymmetrical patterns of ocelli it has been shown that selection can alter not only the amount of precursor but also its distribution along the antero-posterior gradient, although it cannot modify its distribution along a gradient from left to right.

K. C. Sondhi

Department of Zoology,
University College,
London.

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FORTHCOMING EVENTS

(Meetings marked with an asterisk • are open to the public

Monday, January 23

UNIVERSITY OF LONDON (in the Assembly Hall, Institute of Education, Malet Street, London, W.C.1), at 5.15 p.m.—Mr. J. S. Fulton: "The Development of the Newer Universities".•

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE (in the Council Room (second floor) of the Science Museum, Exhibition Road, South Kensington, London, S.W.7), at 5.30 p.m.—Dr. H. R. Calvert: "The History of Mathematical Computers".

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. E. H. S. Burhop: "The Techniques of High Energy Physics"• (Inaugural Lecture).

UNIVERSITY OF LONDON (in the Hatton Lecture Theatre, Queen Mary College, Mile End Road, London, E.1), at 5.30 p.m.—Prof. David C. White (Massachusetts Institute of Technology): "Electrical Energy Conversion".• (Further lectures on January 24 and 26.)

CEMENT AND CONCRETE ASSOCIATION, PRE-STRESSED CONCRETE DEVELOPMENT GROUP (at the Friends House, Euston Road, London, N.W.1), at 6 p.m.—Prof. T. Y. Lin (University of California): "A Review of Advances in Prestressed Concrete in the U.S.A.".

INSTITUTION OF MECHANICAL ENGINEERS, LUBRICATION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Informal Discussion on "Co-ordination of Experimental Work—an Attempt to Determine whether Lubrication Investigations Carried Out by different Bodies can be Integrated".

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Dr. James Taylor: "Towards a Philosophy of the Modern Chemical Industry". (First of three Cantor Lectures on "The Modern Chemical Industry in Great Britain".)

UNIVERSITY OF LONDON (at Birkbeck College, Malet Street, London, W.C.1), at 6 p.m.—Dr. S. Biesheuvel (Johannesburg): "Problems of Cross-cultural Ability Testing".

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (at Savoy Place, London, W.C.2), at 6.30 p.m.—Mr. G. A. Williams: "Economic Heating by Electrode Boilers in Industry".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at Enfield Technical College, Queensway, Ponder's End), at 7 p.m.—Prof. R. L. Wain, F.R.S.: "Chemical Control of Plant Diseases".

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 7 p.m.—Dr. R. C. Rainey: "Locust Control from the Air".

Tuesday, January 24

INSTITUTION OF CHEMICAL ENGINEERS, SOUTH-EASTERN BRANCH (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 3.30 p.m.—Inaugural Meeting.

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Prof. R. Edgeworth Johnstone: "A Survey of Chemical Engineering Education and Practice".

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Machine-Tool Control" opened by Dr. E. H. Frost-Smith.

PARLIAMENTARY AND SCIENTIFIC COMMITTEE, GENERAL COMMITTEE (at the House of Commons, London, S.W.1), at 5.30 p.m.—Meeting with Vice-Chancellors of certain universities.

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. R. S. Lenk: "Papers from Non-Cellulosic Fibres".

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 7 p.m.—Mr. A. A. Fyall, Mr. D. C. Jenkins and Mr. R. N. C. Strain: "Some Problems of Impact and Erosion in Flight".

Wednesday, January 25

INSTITUTE OF PHYSICS and the PHYSICAL SOCIETY, COLOUR GROUP (at Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 3 p.m.—Mr. F. Pollak: "Some Properties of Coloured Half-tone Images"; Dr. J. Hughes: "Colour Xerography".

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. L. R. Tarlo: "Middle and Upper Devonian Psammosteids from Scotland"; Dr. W. D. I. Rolfe: "The Geology of the Hagshaw Hills Silurian Inlier, Lanarkshire".

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. W. E. Willshaw: "Generation and Amplification in the Millimetre Wave Field".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. R. H. Mole: "Radioactive Isotopes and Teeth".• (First of three lectures on "The Scientific Basis of Dentistry" organized by the British Postgraduate Medical Federation.)

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Prof. W. R. Hawthorne: "The Early Development of the 'Dracone' Flexible Barge" (Thomas Lowe Gray Lecture).

SOCIETY OF CHEMICAL INDUSTRY (joint meeting of the FOOD GROUP and OILS AND FATS GROUP, at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Prof. A. C. Frazer: "Some Biological Effects of Heated Fats".

BRITISH INSTITUTION OF RADIO ENGINEERS, ELECTRO-ACOUSTICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. K. R. McLachlan: "Noise Correlation Measurements".

SOCIETY FOR ANALYTICAL CHEMISTRY, MICROCHEMISTRY GROUP (at "The Feathers", Tudor Street, London, E.C.4), at 6.30 p.m.—Discussion Meeting on "Hydrogenation Methods in Microanalysis" opened by Mr. R. A. D. Smith.

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the SLOUGH COLLEGE SCIENTIFIC SOCIETY, at the Slough College of Further Education, William Street, Slough), at 7.30 p.m.—Prof. R. S. Nyholm, F.R.S.: "Magnetism in Inorganic Chemistry".

BRITISH PSYCHOLOGICAL SOCIETY, MEDICAL SECTION (at the Royal Society of Medicine, 1 Wimpole Street, London, W.1), at 8.15 p.m.—Annual General Meeting, followed by Mr. S. H. Foulkes: "Psychotherapy 1961" (Chairman's Address).

Thursday, January 26

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. D. Bloor, Mr. T. J. Dean, Mr. G. O. Jones, Mr. D. H. Martin, Mr. P. A. Mawer and Mr. C. H. Perry: "Spectroscopy at Extreme Infra-Red Wave-lengths"; Mr. G. O. Jones, Mr. D. H. Martin, Mr. P. A. Mawer and Mr. C. H. Perry: "The Lattice Resonances of Ionic Crystals".

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. E. S. Maurer: "Flowers and Perfumes"; Dr. S. M. Manton, F.R.S.: "Evolutionary Paths to Success Among the Millipedes".

UNIVERSITY OF LONDON (at Westfield College, Kidderpore Avenue, Hampstead, London, N.W.3), at 5.15 p.m.—Prof. E. H. Sondheimer: "The Mathematical Description of Nature"• (Inaugural Lecture).

UNIVERSITY OF LONDON (in the Bearsted Theatre, London Hospital Medical College, Turner Street, London, E.1), at 5.30 p.m.—Dr. F. C. Fraser: "Adaptations in Cetaceans".•

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. W. V. Mayneord: "Radioactivity of the Human Environment".• (Fifth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

UNIVERSITY OF LONDON (at the School of Pharmacy, Brunswick Square, London, W.C.1), at 5.30 p.m.—Prof. T. Vályi-Nagy (Debrecen, Hungary): "Pharmacology of Antibiotics".•

INSTITUTION OF MECHANICAL ENGINEERS, APPLIED MECHANICS GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Informal Discussion on "Applications of Electronic Computers in the Study of Applied Mechanics and Electronic Computing in Engineering Design".

Friday, January 27

INSTITUTION OF MINING ENGINEERS (at the Royal Institution of Naval Architects, 10 Upper Belgrave Street, London, S.W.1), at 11.15 a.m.—67th Annual General Meeting. Mr. R. A. Moore: Presidential Address.

INSTITUTE OF RURAL LIFE AT HOME AND OVERSEAS (at Friends International Centre, 32 Tavistock Square, London, W.C.1), at 1.15 p.m.—Dr. Wallace Aykroyd: "The Work and Objectives of F.A.O.".•

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. P. B. Medawar, F.R.S.: "Principle and Paradox in Eugenics" (The Woodhull Lecture).

Saturday, January 28

BIOCHEMICAL SOCIETY (in the Courtauld Hall, Queen Elizabeth College, Campden Hill Road, London, W.8), at 10.25 a.m.—402nd Meeting.

LONDON COUNTY COUNCIL (at the Horniman Museum, London Road, Forest Hill, London, S.E.23), at 3.30 p.m.—Miss F. Hall: "Animal Courtship".•

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT, Grade B (with a good honours degree in physics) IN THE DEPARTMENT OF PHYSICS AND MATHEMATICS—The Principal, College of Further Education, Flatt Walks, Whitehaven, Cumberland (January 27).

ASSISTANT (with some knowledge of fresh-water biology and chemistry) IN THE FISHERIES AND POLLUTION DEPARTMENT, for duties which will include the inspection of sewage works and trade waste treatment plants, river surveys, and the examination of samples.—The Chief Engineer, Somerset River Board, The Watergate, West Quay, Bridgwater, Somerset (January 30).

ASSISTANT LECTURER IN PHYSICS—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (January 31).

ASSISTANT LECTURER OR LECTURER IN ORGANIC CHEMISTRY—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (January 31).

EXAMINER (with a first- or second-class honours degree (or equivalent) in chemistry and two years experience in chemistry) OF APPLICATIONS FOR PATENTS—The Secretary, Civil Service Commission, 45 Upper O'Connell Street, Dublin, Republic of Ireland (January 31).

LECTURER (medical graduate, with experience in virology and in research methods) IN BACTERIOLOGY—The Secretary, The University, Edinburgh (January 31).

LECTURER or ASSISTANT LECTURER IN INORGANIC CHEMISTRY—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (February 3).

RESEARCH WORKER (graduate, familiar with numerical methods and computers), to study calculations performed in the shipbuilding industry and to construct programmes for an automatic computer—The Director, University Computing Laboratory, 1 Kensington Terrace, Newcastle upon Tyne 2 (February 4).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN BIOCHEMISTRY, CHEMISTRY, CIVIL ENGINEERING or PHYSICS—The Registrar, Trinity College, Dublin, Ireland (February 12).

PROFESSOR OF MATHEMATICS (EITHER PURE OR APPLIED)—The Registrar, The University, Leeds 2 (February 14).

READER IN EXPERIMENTAL PATHOLOGY at the Institute of Cancer Research, Royal Cancer Hospital—The Academic Registrar, University of London, Senate House, London, W.C.1 (February 16).

HEAD (with good academic qualifications, with teaching and/or industrial experience) OF THE DEPARTMENT OF APPLIED CHEMISTRY—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1 (February 17).

LECTURER (with at least a good honours degree in geography, and preferably with experience of teaching geography in a university department) IN GEOGRAPHY at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, February 17).

RESEARCH FELLOW IN THE DEPARTMENT OF PHYSIOLOGY, John Curtin School of Medical Research, Australian National University, to work in the field of neurophysiology—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 17).

READER IN MICROBIOLOGY at Queen Elizabeth College—The Academic Registrar, University of London, Senate House, London, W.C.1 (February 21).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOW IN BIOCHEMISTRY, CHEMISTRY, ENGINEERING, PHARMACOLOGY or PHYSICS or related subjects—The Secretary, The University, Aberdeen (February 25).

ASSISTANT LECTURER (honours graduate) IN PHYSICS; and ASSISTANT LECTURERS (2) (honours graduates) IN BOTANY—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (February 28).

ASSISTANTS (2) ONE IN MATHEMATICS and ONE IN STATISTICS—The Secretary of University Court, The University, Glasgow (February 28).

RESEARCH FELLOW IN MATHEMATICS—The Secretary of University Court, The University, Glasgow (February 28).

SENIOR LECTURER (with high mathematical qualifications and preferably previous experience in working with a digital computer) IN MATHEMATICS at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, February 28).

LECTURER IN PHILOSOPHY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, March 4).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN CHEMISTRY or PHYSICS—The Registrar, The University, Hull (March 7).

LECTURERS (2) IN ENGINEERING MATHEMATICS—The Secretary, The Queen's University, Belfast, Northern Ireland (March 10).

LECTURER (with an honours degree in metallurgy or a related subject, or with equivalent qualifications) IN CHEMICAL AND PROCESS METALLURGY at the Wollongong Division (University of New South Wales)—The Agent-General for New South Wales, 56 Strand, London, W.C.1, and the Appointments Section, University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia (March 30).

ASSISTANT DIRECTOR (with a good science degree, preferably with some knowledge of genetics and/or statistics, and a knowledge of at least two foreign languages) OF THE BUREAU OF ANIMAL BREEDING AND GENETICS, King's Buildings, West Mains Road, Edinburgh 9—The Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, Bucks (March 31).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN BIOCHEMISTRY, CHEMISTRY, CHEMOTHERAPY, ENGINEERING, METALLURGY, PHARMACOLOGY or PHYSICS—The Academic Registrar, University of London, Senate House, London, W.C.1 (April 15).

ASSISTANT BIOCHEMIST (with a first- or second-class honours degree in chemistry or biochemistry) IN THE AREA PATHOLOGY LABORATORY based at Stoke Mandeville Hospital—The Administrative Officer, Stoke Mandeville Hospital, Aylesbury.

ASSISTANT EXPERIMENTAL OFFICER (with a pass degree in zoology or bacteriology and preferably experience in serology), for work in the Serology Section—The Secretary, Research Institute, Pirbright, Surrey.

ASSISTANT or ASSOCIATE PROFESSOR (with an honours degree in mathematics and preferably some postgraduate experience in research or teaching) IN THE DEPARTMENT OF MATHEMATICS—Head, Department of Mathematics, University of New Brunswick, Fredericton, N.B., Canada.

CHAIR OF PHARMACY—The Secretary, The Royal College of Science and Technology, George Street, Glasgow, C.1.

CHEMIST (with a first- or second-class honours degree in chemistry or equivalent qualification, and preferably experience in the inorganic analytical field and a knowledge of geochemical techniques) in Nyasaland, to take charge of the Geological Survey Department's chemical laboratory and to undertake assaying and chemical testing of rocks, including full silicate rock analyses—The Director of Recruitment, Colonial Office, London, S.W.1, quoting B/D.105/4/04.

EXPERIMENTAL OFFICERS (2) (graduates in physics or chemistry and interested in research in the field of high temperature gas dynamics), for plasma jet research—Head of the Aeronautics Department, Imperial College of Science and Technology, London, S.W.7.

PHARMACOLOGIST, BIOCHEMIST or ORGANIC CHEMIST with biological experience (Ph.D. standard), for work in the field of chemotherapy—The Secretary, Medical Research Council of Ireland, 50 Merrion Square, Dublin, Republic of Ireland.

RESEARCH ASSISTANT (preferably graduate, with laboratory experience in chemistry or biochemistry), for work on amino-acid metabolism—Dr. L. I. Woolf, Department of Regius Professor of Medicine, Radcliffe Infirmary, Oxford.

SENIOR SCIENTIFIC OFFICER (with a good honours degree in one of the following: agriculture, chemistry or biochemistry, with at least two years research experience), to act as Secretary of a proposed Research and Development Committee which will be concerned with problems relating to the growing, harvesting, handling and marketing of potatoes—Establishment Officer, Potato Marketing Board, 50 Hans Crescent, Knightsbridge, London, S.W.1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The British Cast Iron Research Association. Thirty-ninth Annual Report for the year ending 30th June, 1960. Pp. 55. (Alvechurch, Birmingham: British Cast Iron Research Association, 1960.) [2410

Association of Universities of the British Commonwealth. United Kingdom Postgraduate Awards, 1960–62: Fellowships, Scholarships, Grants, etc., tenable at universities in the United Kingdom. Short list of awards tenable outside the United Kingdom. Tenth edition. Pp. ii+136. (London: Association of Universities of the British Commonwealth, 1960.) [2610

Scientific Council for Africa South of the Sahara. CSA/CCTA. Publication No. 52: CSA Meeting of Specialists on Open Forests in Tropical Africa, Ndola, Northern Rhodesia. Pp. 126. (London: Bureau of Publications, CCTA/CSA Secretariat, Watergate House, York Buildings, W.C.2, 1960.) [2610

Colonial Office. Report of the Public Services Conferences held in the Colonial Office, London, 1st to 10th March, 1960. Pp. iii+25. (Colonial No. 347). 3*s*. 6*d*. net. Service with Overseas Governments. Pp. 22. (Cmnd. 1193). 1*s*. 3*d*. net. (London: H.M. Stationery Office, 1960.) [2710

Other Countries

Ceylon. Administration Report of the Director of National Museums for 1959. Pp. 51+3 plates. (Colombo: Government Publications Bureau, 1960.) Rs. 1.50. [2410

Population Reference Bureau, Inc. *Population Bulletin*, Vol. 16, No. 7: Fertility Cult: U.S.A. Pp. 133–150. (Washington, D.C.: Population Reference Bureau, Inc., 1960.) 50 cents. [2410

Tea Research Institute of East Africa. Annual Report for the year 1959. Pp. 40. (Kericho: Tea Research Institute of East Africa, 1960.) [2410

Proceedings of the California Academy of Sciences. Vol. 30, No. 1 (September 30, 1960): Investigations in the Natural History of Baja California. By Ira L. Wiggins. Pp. 1–45+4 plates. (San Francisco: California Academy of Sciences, 1960.) [2410

United States Department of the Interior: Geological Survey. Professional Paper No. 400-A: Geological Survey Research 1960—Synopsis of Geological Results. Pp. xii+136. Professional Paper 400-B: Geological Survey Research 1960—Short Papers in the Geological Sciences. Pp. viii+515. 4.25 dollars. (Washington, D.C.: Government Printing Office, 1960.) [2410

Chicago Natural History Museum. Fieldiana: Anthropology, Vol. 51, No. 2: Table Rock Pueblo, Arizona. By Paul S. Martin and John B. Rinaldo. Pp. ii+131–298. 5.50 dollars. Fieldiana: Geology, Vol. 14, No. 2: A New Specimen of *Desmatochelys lowi* Williston—a Primitive Cheloniid Sea Turtle from the Cretaceous of South Dakota. By Rainer Zangerl and Robert E. Sloan. Pp. 7–40+2 plates. 1 dollar. Fieldiana: Geology Memoirs, Vol. 3, No. 5: The Vertebrate Fauna of the Selma Formation of Alabama. Part 5: An Advanced Cheloniid Sea Turtle. By Rainer Zangerl. Pp. ii+281–361+plates 30–34. 3.50 dollars. Vol. 42, No. 7: Philippine Zoological Expedition, 1946–1947. Camptopterohelea—a New Genus of Ceratopogonidae from the Philippines. By W. W. Wirth and A. A. Hubert. Pp. 89–91. 10 cents. (Chicago: Chicago Natural History Museum, 1960.) [2410

Jamaica, Banana Board Research Department, Occasional Bulletin No. 2: Breeding the Immune Banana. By R. E. Osbourne. Pp. 8. (Kingston: Government Printer, 1960.) [2410

Jamaica: Ministry of Agriculture and Lands. Fifty Years of Cattle Breeding and Development. Pp. 16. Annual Report of the Ministry of Agriculture and Lands for the year ended 31st December, 1958. Pp. 92. 4*s*. (Kingston: Ministry of Agriculture and Lands, 1960.) [2410

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APPOINTMENTS VACANT

REPUBLIC OF THE SUDAN

The Ministry of Education invites applications from suitably qualified candidates for the following posts in the Khartoum Technical Institute:

(1) Assistant Head of Mechanical Engineering Department.

(2) Assistant Head of Civil Engineering and Building Department.

(3) Senior Lecturers in the following subjects:
(a) Architecture.
(b) Thermodynamics.
(c) Electrical Power and Machines.
(d) Hydraulics.
(e) Theory of Machines.
(f) Accountancy.

(4) Lecturers in the following subjects:
(a) Electrical Power and Transmission.
(b) Strength of Materials.
(c) Heat Engines.
(d) Theory of Machines.
(e) Workshop Technology.
(f) Building Construction.
(g) Building Science.
(h) Building Geometry.
(i) Accountancy.
(j) Physics (Electricity and Magnetism).
(k) Pure and Applied Mathematics.
(l) English Language.

(5) Teachers in the Girls Secretarial School in either:
(a) English Typing,
or (b) Pitman's Shorthand.

Candidates for posts (1) and (2) should possess a University Degree plus appropriate professional qualifications (i.e., A.M.I.C.E. or A.M.I.Mech.E.) and have had teaching experience up to Higher National Certificate Level.

Candidates for posts (3) and (4) should possess a University Degree or appropriate professional qualifications. In the case of posts (4i), (4k) and (4l) candidates must possess previous teaching experience to the "A" level G.C.E.

Candidates for post (5) must possess a recognized Teachers' Diploma in Secretarial Work.

Appointment will be on contract (with bonus) for a period up to five years. Salary scale ranges from £S.1,075 to £S.1,675 per annum for Lecturers and from £S.1,075 to £S.1,975 for Senior Lecturers (£S.1 = £1 0s. 6d.). Commencing salary in accordance with age, qualifications and experience. In addition to salary quoted a cost of living allowance, which is reviewed every two months, is payable. The average usually ranges between £S.168 and £S.180 per annum. An initial outfit allowance of £S.50 is payable on appointment. Leave accrues at the rate of seven days per month.

A special resettlement gratuity to British Lecturers teaching in English in Secondary Schools and higher institutions of the Ministry of Education will also be paid on satisfactory completion of the period of contract.

Applications, in writing, stating full details of age, qualifications and experience, should be made to the Appointments Section, Sudan Embassy, Cleveland Row, London, S.W.1.

Closing date: February 15, 1961.

CHEMISTS, MATHEMATICIANS (INCLUDing Statisticians), Physicists, Mechanical and Electrical Engineers (men and women) required for Research and Development Establishments of War Office at various locations including Feltham, Middx.; Sevenoaks, Kent; Byfleet, Chertsey and Tolworth, Surrey; Shoeburyness, Essex; Christchurch and Farnborough, Hants; Salisbury, Wilts.; Cornwall (Chemists only), Anglesey (Mathematicians). Appointments in grade of (a) Senior Scientific Officer (£1,250 to £1,540) or (b) Scientific Officer (£690 to £1,144). Starting salary according to experience. Superannuation under F.S.S.U., with opportunity for candidates under 31 to compete for establishment (pensionable) posts. First- or second-class honours degree or equivalent required, and for (a) minimum age 27 and at least three years' postgraduate research experience.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1. Quote: A.557/OA.

MINISTRY OF POWER, SHEFFIELD, Require Assistant Technical Editor. Work involves editing of reports and papers concerning safety in mines research, script writing for scientific films and copy writing for exhibitions. Post suitable to person between 20 and 30. Minimum qualifications pass degree in science, technology or arts. Starting salary depending on age and qualifications in scale of Assistant Experimental Officer (£440 to £945) or Experimental Officer (£1,045 to £1,285).—Forms and details from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.604/OA.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH CHEMIST OR BIOCHEMIST

(No. 410/89)

The Organization's **Dairy Research Section, Melbourne, Victoria,** invites applications for the position of Research Chemist or Biochemist from Honours Graduates in Science or Agricultural Science to take part in an expanded programme of research on dairy manufacture.

The appointee will be one of a group dealing with the chemistry and technology of butter and butterfat, and will be required to study initially the properties of butterfat which affect its stability towards oxidation and its suitability for baking and food manufacturing purposes generally.

ANIMAL PHYSIOLOGIST

(No. 205/211)

The Organization's **Ian Clunies Ross Animal Research Laboratory Division of Animal Physiology, Sydney, N.S.W.,** invites applications for the position of Physiologist from graduates in Veterinary Science, or Honours graduates in Agricultural Science or Science (majoring in Biology), with at least three years postgraduate research experience to participate in the Laboratory's major research programme on the study of the physiology of reproduction in sheep.

It is now planned to extend this programme to include a study of reproductive performance in the field. The appointee, who will be based at the Laboratory will spend a large part of his time in the field in all States of Australia and will be expected to develop active collaboration with existing field investigators. If necessary, preliminary training in specialist techniques will be given before field work is commenced.

Salary: Dependent on qualifications and experience within the ranges £A.1,510 to £A.2,265 per annum, or £A.2,395 to £A.2,720 per annum.

Salary for women will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further details of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting relevant Appointment number) should be addressed by February 25, 1961.

GRADUATE APPOINTMENTS AT ILLINOIS INSTITUTE OF TECHNOLOGY

Qualified students who wish to begin work leading toward the Doctor of Philosophy degree in the Department of Chemistry during the year 1961-62 are invited to apply. Individual programmes may be selected from the fields of study of quantum chemistry: thermodynamics of non-electrolytic solutions, electrolytes in non-aqueous solutions, and high temperature systems: irreversible thermodynamics: solid state chemistry: applications of ultra-violet and infra-red spectroscopy and nuclear magnetic resonance to chemical problems: chemical physics of polymers: kinetics, reaction mechanisms, acid-base catalysis, and isotope effects: chemistry of the halides and hydrides of boron and of co-ordination compounds: synthesis and stereochemistry of heterocyclic compounds, enzyme and vitamin model compounds, amino-acids, fluorinated compounds, acetylene derivatives and chelating agents, offered by eighteen staff members of the Department. Appointments cover remission of all University costs, laboratory equipment, and chemicals and provide funds sufficient for living expenses, personal needs, and return travel.

For detailed information please write to Professor Arthur E. Martell, Chairman, Department of Chemistry, Illinois Institute of Technology, Chicago 16, Illinois, U.S.A.

SENIOR PSYCHOLOGIST (MALE) REquired for Clothing and Equipment Physiological Research Establishment (War Office), Farnborough, Hants, to investigate problems of human engineering of Guided Weapons, and make recommendations on designs and layouts and experimental evaluation of operators' consoles. The man/machine interactions of all types of fighting vehicles are also studied. Electronic and mechanical knowledge and understanding of background of radar and G.W. systems advantageous. Qualifications: (a) First- or second-class honours degree with psychology as a main subject; (b) higher degree in psychology; (c) postgraduate diploma in psychology following at least two years' systematic study or (d) fellowship of British Psychological Society, or an equivalent qualification. Salary range, £1,193 to £1,495. Minimum age 31.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting G.502/OA. Closing date February 11, 1961.

AUSTRALIA

THE UNIVERSITY OF NEW SOUTH WALES WOLLONGONG DIVISION LECTURER IN METALLURGY

The University invites applications for appointment to the position of Lecturer in Chemical and Process Metallurgy at the Wollongong Division. Salary: £A.1,759 range £A.2,464 per annum. Commencing salary according to qualifications and experience. Applicants must possess an honours degree in metallurgy or related subject, or possess equivalent qualifications. The metallurgical industries in the Port Kembla-Wollongong area are implementing a major expansion programme and the University is introducing a degree course in metallurgy in a new college at Wollongong. Laboratories for the metallurgy section are under construction. Subject to passing a medical examination, appointee will be eligible to contribute to the State Superannuation Fund. First-class ship fares to Sydney of appointee and family will be paid. Further information may be obtained from professor R. H. Myers, Head of the School of Metallurgy, Sydney.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56 Strand, London, W.C.2, and a copy forwarded to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, by airmail to reach there before March 30, 1961. Candidates outside the United Kingdom and Ireland need only submit one copy of their applications to the London address.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Research Assistant in the Computing Machine Laboratory, tenable in the first instance for a period of approximately one year. Applicants should have a degree in mathematics or equivalent qualifications. The person appointed will be required to assist in the operation of a Computing Service on the Mercury and Atlas electronic computers. Previous experience of electronic computers is desirable but not essential. The salary will be according to age and qualifications.

Applications should be sent not later than February 4, 1961, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

ENGLISH ELECTRIC

The Mathematics Group of the Company's Mechanical Engineering Laboratories which are situated in pleasant countryside to the South of Leicester, require a number of

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Please write, giving personal details to : Technical Staff Officer, Dept. G.P.S., English Electric House, Strand, London, W.C.2, quoting reference N 1913F.

UNIVERSITY COLLEGE, DUBLIN

I.C.I. RESEARCH FELLOWSHIPS

Applications are invited for I.C.I. Research Fellowships in Biochemistry, Chemistry or Physics, to which some appointments may be made during the current academic year. The appointments will date from October 1, 1961 (or earlier in the case of a selected candidate who may be available before that date) and will be for one year in the first instance; the maximum period of appointment is three years. The salary will depend upon qualifications and experience and will normally be within the range £800 to £1,100 per annum, together with family allowances.

Applicants should hold a Ph.D. or have equivalent research experience. Applications (three copies; from overseas one will suffice) should give age particulars of training, qualifications, research and other relative experience, a list of publications, an outline of the proposed field of research, and the names of two referees. Applications will be accepted up to March 7, 1961, by the undersigned, from whom a form (of which the use is optional) and other particulars may be obtained.

J. J. HOGAN,
Registrar.

UNIVERSITY OF BIRMINGHAM

LECTURESHIP IN STATISTICS

Applications are invited for the post of Lecturer (£1,050 by £50 to £1,400 by £75 to £1,550; £1,550 by £75 to £1,850) or Assistant Lecturer (£850 by £50 to £950) in Statistics in the Department of Pure Mathematics. The appointment will carry F.S.S.U. and family allowance benefits. The initial stipend will be related to qualifications and experience.

Applications (three copies), with the names of three referees, should be sent by February 15, 1961, to the Registrar, the University, Edgbaston, Birmingham, 15, from whom further particulars may be obtained.

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SCIENCE SPECIALISTS: NATIONAL AGRIcultural Advisory Service, Ministry of Agriculture, Fisheries and Food. Pensionable posts for men and women at least 20½ on April 1, 1961, as specialist advisory officers in soil chemistry, chemistry of animal nutrition, entomology, plant pathology, or bacteriology, and as analysts for work on soils, plants, feeding stuffs, and other agricultural materials. Qualifications: degree (or equivalent) in agricultural science or appropriate natural science. Postgraduate study or research in a relevant subject an advantage. Grade on appointment depends on age, qualifications and experience. Final year students may apply. National salary scales: Grade IV, £718 to £993; Grade III, £1,004 to £1,570; Grade II, £1,576 to £1,914. Starting salary may be above minimum in all grades. Promotion prospects.—Write Civil Service Commission, Burlington Gardens, London, W.1, for application form quoting **296/61**. Closing date February 15, 1961.

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COVENTRY

Applications are invited for the post of Technician in the Department of Applied Physics. Applicants should have experience with laboratory instruments and apparatus and be capable of maintaining and developing laboratory facilities in the Department of Applied Physics. They should also be in a position to give some assistance with similar facilities in the Department of Electrical Engineering. This is a permanent post in the Council's service, with officer's status, monthly salary, superannuation and generous holiday and sick pay scheme. Salary £555 to £925 per annum, plus £26 per annum in certain circumstances on salaries up to £795 per annum. Commencing salary depends on qualifications and experience and will be discussed with candidates selected for interview.

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Applications to Professor H. Ford, Imperial College, London, S.W.7.

THE ROYAL COLLEGE NAIROBI

Applications are invited for the Chair of Mathematics. Salary £3,000 per annum. F.S.S.U. Child allowance £50 per annum per child (maximum £150 per annum). Passages for appointee and family (up to four adult passages) on appointment, termination and leave (once every two years). Rent according to quarters provided £60 to £114 per annum. Medical Scheme for member and family.

Detailed applications (eight copies), naming three referees, by February 28, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

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A vacancy exists in the Technical Staff of the Patents Department of E.M.I. for a University Graduate with a degree in Physics, Mathematics or Engineering to assist in the assessment of new ideas for Patent applications. The successful applicant will be required to work in close cooperation with the various Research and Development teams with particular reference to digital computer techniques. This post offers a good starting salary with considerable prospects for advancement.

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The Personnel Manager,
E.M.I. Ltd.,
Blyth Road,
Hayes, Middlesex.

UNIVERSITY OF ADELAIDE

WAITE AGRICULTURAL RESEARCH INSTITUTE

The University invites applications for appointment at the Waite Institute as Plant Pathologist. Duties: To conduct investigations on the root and stem rots of Wheat. The appointment is financed by a grant from the Wheat Industry Research Council and will be made within the Lecturer salary range of £A.1,675 by £A.95 to £A.2,340 with provision for superannuation on the F.S.S.U. basis. The appointment is for three years in the first instance, renewable annually thereafter as long as it is supported by the Wheat Council. The Waite Institute has excellent facilities in field, glasshouse and laboratory for work in this field, and the lecturer will be associated with a considerable group of colleagues in his own field of study.

Further information about the University and this appointment and the general conditions of appointment can be obtained from the Registrar, the University of Adelaide, Adelaide, South Australia, with whom applications in duplicate, setting out the information specified in the last paragraph of the general conditions (obtainable also from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1) should be lodged not later than February 20, 1961.

UNIVERSITY OF OTAGO

DUNEDIN, NEW ZEALAND

DEAN OF THE FACULTY OF HOME SCIENCE

The University proposes to appoint a Dean of the Faculty of Home Science in succession to Professor Elizabeth Gregory, Ph.D., who is to retire shortly. The Dean to be appointed will also be a Professor in one of the fields covered by the work of the School. The salary is £2,800 per annum.

Further information may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, or from the Registrar, University of Otago, Dunedin, New Zealand. Applications close, in New Zealand and London, on April 30, 1961.

RESEARCH INSTITUTE (ANIMAL VIRUS Diseases), Pirbright, Surrey, invites applications: (1) For an appointment in the Tissue Culture Section. Applicants should have an honours degree in bacteriology or zoology and have experience of culture techniques applied to mammalian tissue. Salary in Principal Scientific Officer grade, £1,600 to £2,325 or Senior Scientific Officer grade, £1,250 to £1,590, depending on age, qualifications and experience. Superannuation under F.S.S.U. House available for married applicant. Applications to the Secretary. (2) From young graduate physicists or physical chemists for a post in the Biophysics Department. The successful candidate will be engaged upon the application of a variety of physical-chemical techniques to the study of viruses and related biological systems, and will be encouraged to work for a higher degree. Current methods of investigations include electronmicroscopy, ultracentrifugation, light scattering and X-irradiation, etc. Interest rather than experience is required at this stage. The appointment will be made according to age and experience in the Scientific Officer grade, £690 to £1,175, or Senior Scientific Officer grade, £1,250 to £1,590. Superannuation under F.S.S.U. House available for married applicant.—Applications to the Secretary.

Bacteriologist

A vacancy has occurred for a qualified Bacteriologist to join a research team in Sandwich, working on an interesting range of veterinary activities.

The post calls for a man preferably with industrial experience, who has been concerned with antibacterials, rumen microbiology and the artificial rumen. A veterinary qualification would be an advantage. Preferred age range 24 to 30.

Conditions of service are of a high standard and include generous non-contributory pension and life assurance schemes. The salary will be attractive. Living areas within reasonable distance of the Sandwich Plant include the Kent coast and Canterbury etc. Removal expenses will be paid and assistance may be provided for house purchase.

Applications are invited : they should be addressed to

THE CHIEF PERSONNEL OFFICER,
PFIZER LIMITED, SANDWICH, KENT

THE Pfizer GROUP
CHEMICALS PHARMACEUTICALS VACCINES
AGRICULTURAL & VETERINARY PRODUCTS

RESEARCH
in GAS PRODUCTION

The Midlands Research Station of the Gas Council, which is situated at Solihull, Warwickshire, is developing new high-pressure methods of town gas production from coal and oil, and invites applications from well qualified chemists, chemical engineers and fuel technologists who would be interested in working on them. There are opportunities both in the laboratory and on pilot plant, some of which is on the largest scale.

Projects include :

1. *Gasification of coals in steam and oxygen, with removal of the ash as molten slag.*
2. *The hydrogenation of powdered coal in fluidized beds or entrained in the hydrogenating gas.*
3. *The hydrogenation of crude petroleum or of petroleum fractions, and of tars, to gas and aromatic by-products.*
4. *The catalytic gasification of light hydrocarbons.*
5. *The catalytic conversion of carbon monoxide with steam under pressure to carbon dioxide and hydrogen.*

Candidates should hold first- or second-class honours degrees or an equivalent professional qualification. Research experience will be an advantage.

Salary will be commensurate with qualifications and experience.

Please write fully to the Industrial Relations Officer.

West Midlands Gas Board, 6 Augustus Road, Edgbaston, Birmingham, 15.

PAINT TECHNOLOGIST

If you have a good University Degree in chemistry with at least seven years' industrial experience in paint and varnish technology, and your age is still under 35, IMPERIAL CHEMICAL INDUSTRIES LIMITED, NOBEL DIVISION, has a vacancy that will interest you. In the Division's Research and Development Department on the Ayrshire Coast of the Firth of Clyde, stimulating work on surface coating agents engages vigorous effort.

The successful candidate will be engaged on the servicing and development of paint and lacquer intermediates for surface coatings.

Starting salary will depend on qualifications and experience. The Company operates a five-day week, a Staff Pension Fund and a Profit-Sharing Scheme. A married man will receive a refund of reasonable removal expenses, and assistance towards house purchase is available.

Applications should be made in writing, direct to the :

Staff Manager,
IMPERIAL CHEMICAL INDUSTRIES LTD.,
Nobel Division,
460 Sauchiehall Street,
Glasgow, C.2.

UNITED KINGDOM ATOMIC ENERGY AUTHORITY

WANTAGE RESEARCH LABORATORY, WANTAGE, BERKS.

requires

Scientists

for the following research appointments :

1. Senior Scientific Officer or Scientific Officer (Ref. 1831/34)
to be responsible for developing microcalorimetric and other methods of absolute measurement of radioactivity and of radiation fluxes, and to supervise a section engaged in the issue of radioactive standards.
Experience of calorimetry and in handling radioactive materials desirable.

2. Senior Scientific Officer (Ref. 1831/A/34)
to investigate the physical effects of gamma radiation and to make associated measurements and calculations. Experience of gamma radiation scattering and dosimetry desirable.

3. Senior Scientific Officer or Scientific Officer (Ref. 1838/34)
to take charge of a small section working on the application of radioactive isotopes to mechanical wear problems. Work includes practical and fundamental investigations.

Significant experience in this work or in metal physics would be an advantage.

Applicants for all posts should have a first- or good second-class honours degree.

Starting salary in the following ranges according to age and experience :

Scientific Officer £755 to £1,250 per annum.
Senior Scientific Officer £1,365 to £1,675 per annum.

Housing and superannuation schemes.

Send post card for details to the Personnel Manager (quoting appropriate Ref. No.), A.E.R.E., Harwell, Didcot, Berks.

GRADUATES REQUIRED, PREFERABLY with experience in research on free radicals, photochemistry, semi-conductors or allied fields to join research team ; also assistant chemists of H.N.C. standard for a variety of interesting investigations in a rapidly expanding private research organization. Good prospects for the right people. Five-day week, pension scheme.—Write for application form to the J. A. Radley Research Institute, 220 Elgar Road, Reading, Berks.

CENTRAL HISTOLOGICAL LABORATORY, Whittington Hospital, Archway Wing, London, N.19. Senior Technician I or Technician required. Practical experience in the preparation and mounting of museum specimens essential ; some knowledge of photography an advantage.—Applications, stating age, qualifications and experience, with the names of two referees, to the Group Secretary, Archway Group H.M.C., 46 Cholmeley Park, N.6, by January 30, 1961.

ASSISTANT EXPERIMENTAL OFFICER required by Research Institute, Pirbright, for work in Serology Section. Qualifications : Pass degree in zoology or bacteriology, experience in serology an advantage. Salary according to age in scale from £600 at age 22, rising to £945.—Applications to Secretary.

AUSTRALIAN NATIONAL UNIVERSITY

INSTITUTE OF ADVANCED STUDIES
DEPARTMENT OF MATHEMATICS

Applications are invited for appointments in all grades in the newly established Department of Mathematics in the Research School of Physical Sciences. The Department will be concerned with research, and training in research, initially in pure mathematics; it will be headed by Dr. B. H. Neumann, F.R.S., Professor-Elect. The appointments will be made at levels appropriate to the qualifications and experience of the successful candidates. Superannuation is on the F.S.S.U. pattern. Reasonable travel expenses are paid and assistance with housing is provided.

A summary of conditions of appointment, including the types of posts available with the appropriate salaries, is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on February 20, 1961.

UNIVERSITY OF DURHAM

THE MEDICAL SCHOOL, KING'S COLLEGE
NEWCASTLE UPON TYNE

The Council of King's College invite applications from suitable qualified graduates in medicine or science for the post of Research Assistant in the Department of Anaesthetics. Physiological knowledge and experience in simpler biochemical estimations would be of value. Commencing salary will be at a suitable point on the salary grade for Clinical Medical Research Assistants (£1,300 to £2,150) or on the Non-medical Research Assistants grade (£1,050 to £1,850) according to qualifications and experience. Family allowances and F.S.S.U.

Applications (twelve copies), together with the names and addresses of three persons to whom reference may be made, should be submitted not later than February 18, 1961, to the Registrar and Secretary of King's College.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF MATHEMATICS

Applications are invited for the post of Reader in Applied Mathematics. Salary scale: £1,800 by £50 to £2,100 per annum, plus London allowance of £38 or £51 according to age.

Information about the Department, together with further particulars of the post, may be obtained from the Clerk to the Governors. Applications by February 15, 1961.

DEPARTMENT OF GEOPHYSICS

UNIVERSITY OF WESTERN ONTARIO, LONDON, CANADA

Applications are invited for the position of Lecturer or Assistant Professor. Applicants should possess a Ph.D. or equivalent. Inquiries are also invited from persons wanting to carry out graduate research leading to a higher degree. Facilities are available for research in Terrestrial Heat Flow, Seismology, High Pressure Phenomena, Rock Magnetism, Nuclear Geology, Gravitation, Exploration Geophysics.

Lists will be closed on March 15, 1961, or when the positions are filled, whichever is the earlier. Inquiries should be addressed to the Head of the Department.

SENIOR LECTURERS OR LECTURERS IN Physics, Mathematics, Thermodynamics required by Royal Military College of Science, Shrivenham, Berks, to lecture to London external degree courses (and possibly specialized courses) and assist with laboratory classes. Teaching is at University level. There are extensive well-equipped laboratories; research is encouraged and work would be suitable for publication and submission for higher degree. Qualifications: First- or second-class honours degree or equivalent, preferably with teaching and/or research experience. Physicist expected to engage in research in nuclear, radiation or solid state physics. Mathematician should have interest in applied mathematics. Thermodynamics posts (2) require suitable practical experience; selected candidates expected to undertake or supervise research in thermodynamics or gas dynamics. Salary ranges: Senior Lecturer, £1,250 to £1,540; Lecturer, £695 to £1,144. Credit given for postgraduate experience and National Service in determining starting salary. Superannuation under F.S.S.U. Good prospects of permanency. Accommodation: residential Officers' Mess for single men, houses for married men.—Particulars and application forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.556/OA.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF CHEMISTRY

Applications are invited for the post of Lecturer or Assistant Lecturer in Inorganic Chemistry. Salary scales: Lecturer, £1,370 by £35 to £1,550; Assistant Lecturer, £700 by £27 10s. to £1,150; plus additions for training (£30 to £120); graduate status (£90); good Honours Degree (£75); London allowance of £38 or £51, according to age. The grading of the post will depend upon qualifications and experience.

Further particulars may be obtained from the Clerk to the Governors, by whom applications should be received not later than February 3, 1961.

LEVINGTON RESEARCH STATION

FUNDAMENTAL RESEARCH

A RESEARCH SCIENTIST is required, trained in classical physics, applied mathematics, fluid dynamics, physical or theoretical chemistry or in an engineering science, with research experience and preferably a research degree. The work, loosely described as "fundamental chemical engineering research," will involve theoretical and experimental investigations of processing operations such as transfer of heat, mass, simultaneous heat and mass, and chemical potential to collections of discrete solids and drops; physical action of solid upon solid; fluid mechanics of fluid-solid systems; transient behaviour of well defined flow-systems and of processing plant; and other problems. Experience in one of these is desirable but research training and aptitude, an analytical approach to problems, and fairly high mathematical ability are essential.

The work is a Bramford Development Station (near Ipswich), a physically separate part of Levington Research Station. Pilot plants at Bramford provide continuity between investigations of fundamental, microscopic, concepts and the industrial complex of processes. A laboratory, into which the scientist can incorporate his ideas, is to be furnished, and a library is arising. Additional facilities are available at Levington—library, X-ray and other forms of analysis, electron microscope, and specialized advice on statistical, chemical and physical analysis. Staff are encouraged to publish.

Salary according to experience and qualifications.

The Company operates a Pension Scheme which, for married staff, includes provision for widows and dependent children.

Applications, with full particulars, to Personnel Manager (KN10), Fisons Fertilizers Limited, Harvest House, Felixstowe, Suffolk.

ST. MARY'S HOSPITAL MEDICAL SCHOOL

(UNIVERSITY OF LONDON)
PADDINGTON, W.2

Senior or Junior Research Assistant required for the M.R.C. Research Group in Enzymology in the Department of Chemical Pathology. Salary scales: Senior, £1,510 by £100 to £1,910; Junior, £910 by £50 to £1,210, together with superannuation under F.S.S.U.

Applications, together with the names of two referees, should be sent to the School Secretary, by February 4, 1961.

KENT EDUCATION COMMITTEE

MEDWAY COLLEGE OF TECHNOLOGY
DEPARTMENT OF SCIENCE

A Lecturer in Paper Technology required, to commence duties as soon as possible. Candidates should have graduate qualifications and wide experience of the paper-making industry. The successful candidate will be responsible to the Head of Department for organization and development of courses in Paper Technology, including a block release course which is to commence in April, 1961. Salary in accordance with the Burnham Technical Scale for Lecturers.

Further particulars and application forms may be obtained from the Principal, Medway College of Technology, Horsted, Maidstone Road, Chatham, Kent, to whom completed forms should be returned within fourteen days.

COMMONWEALTH AGRICULTURAL BUREAUX

Applications are invited for a vacancy as Junior Mycologist at the Commonwealth Mycological Institute, Kew, from candidates with a good honours degree in botany, and postgraduate training in systematic mycology. A working knowledge of Latin and German is required, with Russian an added qualification. Salary scale £710 to £2,325 by annual increments with bars and an additional London weighting of £20 to £50. Starting salary according to age, qualifications and experience. For those aged 32 or under at time of appointment, up to two increments allowed for completed years of National Service and two extra increments after two years' satisfactory service. Provision for superannuation.

Further information from the Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, Bucks, England, to whom applications should be made not later than March 31, 1961. Government employees should apply through their Governments.

SOUTH DEVON AND EAST CORNWALL HOSPITAL

AREA PATHOLOGICAL LABORATORY, GREENBANK ROAD, PLYMOUTH

Applications are invited from suitably qualified persons for the post of Non-medical Biochemist, Senior Grade, in this Laboratory.

Applications, stating age, nationality, qualifications, experience and names of three referees, to Group Secretary, 7 Nelson Gardens, Stoke, Plymouth.

UNIVERSITY OF MANITOBA

DEPARTMENT OF PHYSICS

Applications are invited for positions as (1) Professor (minimum salary $12,000 per annum) (2) Associate Professor (minimum salary $9,000 per annum). Persons sought are those with high qualifications in experimental nuclear physics, preferably, though not necessarily, with cyclotron experience, to work with the 50 MeV. sector-focused cyclotron now under construction in this Department. Appointments will be to the full-time academic staff, and will involve some teaching, but emphasis will be placed on the development of the cyclotron research programme.

For further information apply to Dr. B. G. Whitmore, Head, Physics Department, University of Manitoba, Winnipeg, Manitoba, Canada.

UNIVERSITY OF DURHAM

COMPUTING LABORATORY
NEWCASTLE UPON TYNE

A research worker is required to study calculations performed in the shipbuilding industry and to construct programmes for an automatic computer. Applicants should be graduates and familiar with numerical methods and computers, but previous knowledge of shipbuilding is not essential. The post which is being financed by the British Shipbuilding Research Association is for three years. Salary in the range £850 by £50 to £1,050 per annum, plus F.S.S.U.

Applications, giving details of qualifications and experience and the names of two referees, should reach the Director, University Computing Laboratory, 1 Kensington Terrace, Newcastle upon Tyne 2, not later than February 4, 1961.

REGISTRAR,
University Office,
46 North Bailey,
Durham.

SOUTH WARWICKSHIRE HOSPITAL GROUP

Biochemist (Principal Grade) required to take charge of the Biochemical Department of the Group Laboratory, Lakin Road, Warwick. The appointment, which is under Whitley Council scales and conditions, will be vacant in April. Hospitals may be visited by candidates.

Applications, giving age, details of experience and qualifications and the names of three referees, to Group Secretary, 50 Holly Walk, Leamington Spa, by February 18, 1961.

FELLOWSHIPS AND ASSISTANTSHIPS for advanced degree students in the fields of metallurgy, ceramics and semiconductors. A new Materials Research Centre provides exceptional facilities for basic research and graduate studies in kinetics physical ceramics and metallurgy, imperfection studies in solids, physics of solids, thermodynamics and X-ray diffraction.—Applicants with degrees in mathematics, the physical sciences or engineering will be considered. Department of Materials Science, the Technological Institute, Evanston, Illinois.

WARWICKSHIRE EDUCATION COMMITTEE

RUGBY COLLEGE OF ENGINEERING TECHNOLOGY

WARDEN OF HALLS OF RESIDENCE

Applications are invited for the post of Warden of the Faraday and Newton Halls for 100 men students. The Warden is a member of the teaching staff and must be qualified to teach engineering and science students attending Diploma in Technology and Degree courses. (Teachers of Liberal Studies are invited to apply.) Salary scale: £1,550 by £50 to £1,750. The Warden will be required to reside in the Warden's House, and will be granted free residence (including heating and lighting).

Further particulars and application forms may be obtained from the Principal, Rugby College of Engineering Technology, Eastlands, Rugby, to whom completed forms must be returned not later than February 3, 1961.

N. A. Y. YORKE-LODGE,
County Education Officer.

BRITISH TITAN PRODUCTS COMPANY LIMITED

RESEARCH STUDENTSHIP IN INORGANIC CHEMISTRY

Applications are invited for the above studentship, which will become vacant on October 1, 1961. Candidates will be expected to conduct independent research in some branch of inorganic chemistry. They should be normally resident in the U.K. and be British subjects. They should have completed the degree of Ph.D. The emolument will be £850 and the tenure usually three years. Applications should be submitted before March 6, 1961.

Further details can be obtained from Dr. F. B. Kipping or Dr. A. G. Sharpe at the University Chemical Laboratory, Lensfield Road, Cambridge.

OLDCHURCH HOSPITAL ROMFORD, ESSEX

(709 Beds)

RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

Honours graduate in chemistry or biochemistry required in Radiobiochemistry Department for biochemical research involving the use of radioactive isotopes and in particular C^{14} and tritium. The appointment will be made in the grade of Scientific Officer (£717 to £1,222) or of Senior Scientific Officer (£1,302 to £1,654) at a salary commensurate with experience and qualifications; F.S.S.U. Facilities exist to register for higher degree.

Applications, naming two referees, to the Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/1.

THE LABORATORY OF BACTERIOLOGY of Cornell University invites applications for Teaching and Research Assistantships. Applicants must be qualified to work for an advanced degree (M.S. or Ph.D.) in Bacteriology, although prior bacteriology training is not required. Stipends are usually in the range of $2,200 to $3,200 per annum. Applications for the academic year 1961-62 should be completed by April.—Further details and information may be obtained from Professor E. A. Delwiche, Laboratory of Bacteriology, Cornell University, Ithaca, New York, U.S.A.

UNIVERSITY OF WESTERN ONTARIO, London, Canada: N.R.C. postdoctoral Research Fellowship with preference for structural geology but other fields considered if candidate has satisfactory qualifications. Stipend is $4,000 single, $5,000 married, tax free, plus travel and generous equipment allowance. Application blanks, and information from Chairman, Geology Department. Closing date May 1, 1961.—Applications from candidates for graduate degrees also received until April 1.

AUSTRALIAN NATIONAL UNIVERSITY

INSTITUTE OF ADVANCED STUDIES
JOHN CURTIN SCHOOL OF MEDICAL RESEARCH

Applications are invited for appointment as Research Fellow to work in the field of neurophysiology in the Department of Physiology. The salary will be within a range, at present £A.1,437 to A.2,152, which is under review. Appointment will be for three years, with possible extension to a maximum of five years. Superannuation is on the F.S.S.U. pattern. Reasonable travel expenses are paid, and assistance with housing is provided.

Further particulars are available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on February 17, 1961.

INSTITUTE OF DENTAL SURGERY

(UNIVERSITY OF LONDON)

Eastman Dental Hospital, Gray's Inn Road, London, W.C.1

Workshop technician required for experimental apparatus and prototype construction in Materials Research Laboratory. Salary, for appropriate qualifications, on the scale £620 to £745 per annum with London weighting.

Applications in writing to Jack R. Tayler, Secretary to the Board, as soon as possible.

PILKINGTON BROTHERS LIMITED

require an

ELECTRICAL ENGINEER

to take charge of the High Voltage Laboratory comprising power frequency and impulse test sections with test voltages of up to 1,300 kV. and 2,000 kV. respectively. An intensive programme of research and development relating to toughened glass power line insulators is in progress.

Applications, stating age, qualifications, experience and present salary, should be addressed to the Personnel Officer (Graduate Recruitment), Pilkington Brothers Limited, St. Helens, Lancashire.

UNITED KINGDOM TECHNICAL ASSISTANCE

Applications are invited for the posts of: (1) Expert in Veterinary Pharmacology, (2) Expert in the Anatomy of Domesticated Animals, at the College of Veterinary Science and Animal Husbandry, Uttar Pradesh Mathura, India. Applicants should have for (1) University degree or diploma in veterinary science with postgraduate degree or diploma in veterinary pharmacology. (2) University degree or diploma in veterinary science with postgraduate degree or diploma in veterinary anatomy. Ten years' teaching experience and extensive research work for both posts. Salaries £2,500 per annum, plus generous tax free allowances. Duration two years.

For further information and application form, write to Ministry of Labour (E9), 26 King Street, London, S.W.1, quoting E9/TCS/IND/(1) 893 or (2) 894.

TECALEMIT LIMITED, PLYMOUTH, Devon, have a vacancy for the post of Physicist or Technologist in their Laboratory for testing non-metallic materials. Applications are invited from men under 30 years of age with a University degree who have not less than three years industrial or research experience, preferably connected with one of the following materials: plastics, filter media, rubber and adhesives. The selected candidate will find interesting and varied work in the congenial atmosphere of a modern and expanding factory. The Company offers a contributory Pension-Life insurance scheme, together with a comprehensive range of welfare and recreational activities.—Please apply, in strictest confidence, to the Personnel Manager, giving age, together with qualifications, experience and present salary.

BIRMINGHAM (DUDLEY ROAD) GROUP OF HOSPITALS

DUDLEY ROAD HOSPITAL,
BIRMINGHAM, 18 (775 BEDS)

Applications are invited for the appointment of whole-time Biochemist (Top Grade) in the Group Laboratory at Dudley Road Hospital. Applicants should be well qualified chemists having wide experience in hospital biochemistry. The successful applicant will be in charge of Biochemical Department responsible to Senior Pathologist. He will be required to provide a full-routine service, to take part in and encourage research in Department and in collaboration with other Departments. The appointment will be in accordance with Whitley Council terms and conditions etc.

Applications, naming three referees, to Group Secretary, Dudley Road Hospital, Birmingham, 18, by not later than February 20, 1961.

ROYAL HORTICULTURAL SOCIETY

Applications are invited for the post of Secretary to the Society. Applications, which will be treated as confidential, should be made by letter, stating age, education, experience, present salary, and when available, and should disclose the applicant's suitability for the post. The names and addresses of two referees should be given. The intention is that the successful candidate should understudy the present Secretary for a short period before his retirement. The Council has no preconceived views as to salary, which will depend upon the accomplishments of the successful candidate.

Applicants, marked "Confidential," should reach the President, the Royal Horticultural Society, Vincent Square, London, S.W.1, if possible before February 1.

UNIVERSITY OF HULL

Applications are invited for appointment to Three Lectureships or Assistant Lectureships in Physics, to date from October 1, 1961. Salary: Lecturer, £1,050 to £1,850 per annum; Assistant Lecturer, £800 to £950 per annum, with placing according to qualifications and experience; F.S.S.U.; and family allowances.

Further particulars may be obtained from the undersigned to whom applications (six copies) should be submitted by February 28, 1961.

W. D. CRAIG,
Registrar.

ROAD RESEARCH LABORATORY (Traffic and Safety Division), Langley, Bucks, requires Senior Scientific Officers/Scientific Officers to carry out Theoretical and Experimental Research on Traffic Flow and Road Safety, including psychological aspects, physics of friction and impact problems, relationship between vehicle design and injuries sustained in road accidents, theoretical problems on traffic and application of electronic computer to these problems. Qualifications: First- or second-class honours degree or equivalent, in appropriate subject for Scientific Officer, with adequate postgraduate research experience and minimum age 26 for Senior Scientific Officer. Salary ranges: Scientific Officer, £710 to £1,175; Senior Scientific Officer, £1,290 to £1,590 (according to experience). Normal prospects of promotion in mid-thirties to Principal Scientific Officer, £1,650 to £2,325, with possibilities of higher posts. Opportunities for early establishment with superannuation whilst under age 31. Laboratory expected to move to new accommodation at Crowthorne, near Bracknell, Berkshire in 1963.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A 286/OA.

D.S.I.R. ROAD RESEARCH LABORATORY, Harmondsworth, Middlesex, requires Civil Engineers, Mathematicians, Statisticians in Senior Scientific and Scientific Officer Grades for work in Tropical Section of Laboratory. Qualifications: First- or second-class honours degree. For senior Scientific Officer posts (minimum age 26) at least three years' postgraduate experience is required, either in research or in a related field. Duties: Concern road building in countries in tropical and sub-tropical belts, involving traffic engineering and the economics of road transport generally, and road safety in these regions. Section is based at Harmondsworth and work involves regular visits overseas with, in some instances, postings for periods of one to two years on specific projects. Salary: Within range Senior Scientific Officer, £1,330 to £1,640; Scientific Officer, £730 to £1,205. Normal prospects of promotion in mid-thirties (range up to £2,375) with possibility of higher posts.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting ref. No. E.512/OA.

AEI

Associated Electrical Industries Limited

INSTRUMENTATION DIVISION

NUCLEAR MAGNETIC RESONANCE

The Scientific Apparatus Sales Department of A.E.I. Instrumentation Division require a CHEMIST or PHYSICIST for applications work in Nuclear Magnetic Resonance and allied techniques. This is interesting work in a new and expanding field. Spectroscopic experience in other fields would be an advantage. Training in the NMR field would be given. Please write for application form quoting reference S.17 to :

Personnel Manager,
Associated Electrical Industries (Manchester) Ltd.
Trafford Park, Manchester, 17

UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF APPLIED MATHEMATICS AND THEORETICAL PHYSICS

Applications are invited for an Assistant Lectureship in the Department, to take office on April 1, 1961, or as soon as possible thereafter. The appointment will be for three years in the first instance, with the possibility of reappointment for two further years. The stipends of University teaching officers are under review. The proposed pensionable stipend is £900 a year, rising by annual increments of £50 to £1,150.

Applications should include a statement of the candidate's published work and the names of two referees, and should reach Dr. F. G. Friedlander, Secretary of the Appointments Committee of the Faculty of Mathematics, Arts School, Bene't Street, Cambridge, not later than February 18, 1961.

UNIVERSITY OF MALAYA IN SINGAPORE

Applications are invited for (i) Lectureship or (ii) Assistant Lectureship in each of the following: Chemistry; Geography; Pure or Applied Mathematics. Salary scales: (i) £1,148 by £49 to £1,442/£1,540 by £56 to £1,820 per annum; (ii) £1,001 by £49 to £1,099 per annum. Entry point according to qualifications and experience. Allowances: expatriation in range £280 to £308 per annum, cost of living (temporary) in range £210 to £560 per annum. Passages for appointee, wife and children under 12 years. Partly furnished house/flat at reasonable rent. Provident Fund Scheme.

Detailed applications (eight copies), naming three referees, by March 31, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY COLLEGE OF WEST INDIES

Applications are invited for a Lectureship in Mathematics. Salary scale (under review): £1,150 by £50 to £1,450 by £75 to £1,900 per annum. Entry point determined by qualifications and experience. Child allowance. F.S.S.U. Unfurnished accommodation at rental not in excess of 10 per cent of basic salary. Up to five full passages on appointment, normal termination and study leave (once every three years).

Detailed applications (six copies), naming three referees, by February 16, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

HUDDERSFIELD COLLEGE OF TECHNOLOGY

Principal: Dr. W. E. Scott, M.B.E.

DEPARTMENT OF CHEMISTRY, COLOUR CHEMISTRY AND DYEING

Required as soon as possible: (1) Lecturer to teach Physical Chemistry to the Dip.Tech. and Grad.R.I.C. standard. (2) Lecturer to teach Inorganic Chemistry to Dip.Tech. and Grad.R.I.C. standard. Good teaching experience, together with research and/or industrial experience, is desirable. Excellent facilities for research. Salary (Burnham Scale): £1,370 by £35 to £1,550 per annum. The commencing salary will depend upon qualifications and experience.

Forms of application and further particulars obtainable from the Principal, to whom applications should be returned without delay.

H. GRAY,
Clerk to the Governors.

UNIVERSITY COLLEGE OF NORTH WALES

BANGOR

DEPARTMENT OF APPLIED MATHEMATICS

Applications are invited for the post of Lecturer or Assistant Lecturer in Applied Mathematics. The salary scale for a Lecturer is £1,050 by £50 to £1,400 by £75 to £1,850, and for an Assistant Lecturer it is £800 by £50 to £950. In addition there are F.S.S.U. benefits and family allowances. The appointment will date from October 1, 1961.

Three copies of the application should reach the undersigned, from whom further particulars may be obtained, not later than February 27, 1961.

KENNETH LAWRENCE,
Secretary and Registrar.

UNIVERSITY OF LEICESTER

LECTURESHIP IN BOTANY

Applications are invited for a Lectureship in Botany with special interest in Genetics. Salary scale £1,050 to £1,850 a year, with F.S.S.U. and family allowances; initial salary dependent on qualifications and experience.

Particulars from the Registrar, to whom applications should be sent by February 10.

UNIVERSITY OF CAMBRIDGE

Applications are invited for a University Demonstratorship in Metallurgy: appointment will be from October 1, 1961. Applications close on March 31, 1961.

Details of duties, salary, etc., may be obtained from Dr. F. B. Kipping, University Chemical Laboratory, Lensfield Road, Cambridge.

UNIVERSITY OF SOUTHAMPTON

WESTLAND READERSHIP IN HELICOPTER ENGINEERING

Applications are invited for this newly established Readership in the Department of Aeronautics and Astronautics. Applicants should be suitably qualified with considerable experience in either helicopter design or vibration theory and the person appointed will be expected to engage in and direct research into some aspect of helicopter or rotary wing science. Salary scale £1,650 by £75 to £2,400 by £25 to £2,425. F.S.S.U. and child allowance.

Further particulars may be obtained from the Secretary and Registrar, the University, Southampton, to whom applications (fourteen copies from U.K. applicants) should be sent before February 28, 1961.

UNIVERSITY OF GLASGOW

RESEARCH FELLOWSHIP IN MATHEMATICS

Applications are invited for a Research Fellowship in Mathematics. Salary scale: £800 to £950 per annum. Initial salary according to experience and qualifications. F.S.S.U. and family allowance benefits.

Applications (three copies), should be lodged, not later than February 28, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court.

UNIVERSITY OF LEEDS

DEPARTMENT OF PHYSICS

Applications are invited for appointment in the Department of Physics as Lecturer or Assistant Lecturer from October 1, 1961, or a date to be arranged at a salary on the scale £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar at £1,550) a year for a Lecturer, or within the range £800 to £950 a year for an Assistant Lecturer, according to age, qualifications, and experience.

Applications (three copies), stating date of birth, qualifications and experience, together with the names of three referees, should reach the Registrar, the University, Leeds, 2 (from whom further particulars may be obtained) not later than February 20, 1961.

GLOVERS (CHEMICALS) LTD., OF LEEDS, require an additional Graduate Chemist for Technical Service and Sales duties in their Southern Area. This comprises West London, South-west London, Southern England, South-western England and South Wales. The company supply surface active agents and chemical specialities to many widely differing industries and an ability by candidates to gain knowledge rapidly is essential. A period of training in Leeds will be necessary. The successful applicant will be expected to reside in the Western or South-western London suburbs. A company car will be provided, there is a good salary and a contributory pension scheme.—Applications in writing, from graduates, of about 30 years of age, detailing their qualifications and experience, should be addressed to V. C. H. Brockwell, 6 Spearl Lane, Heston, Hounslow, Middx.

THE CARBORUNDUM COMPANY LIMITED has a vacancy for a Quality Control Statistician in its Technical Branch at Trafford Park, Manchester. The successful applicant will be required to work on problems of applying statistical quality control methods in the manufacture of the company's various product lines. A good science or mathematics degree is essential. The post offers good prospects with ample scope for advancement. Good working conditions, bonus scheme, and generous pension scheme.—All applications, which will be treated in strict confidence, should include details of age, qualifications and experience, and should be addressed to the Manager, Quality Control Department, Technical Branch, The Carborundum Company Ltd., Trafford Park, Manchester, 17.

THE BRITISH NON-FERROUS METALS Research Association, a leader in the field of specialized information services, is strengthening its Information Department and is about to make a senior and a junior appointment both of which will offer scope for advancement and carry salaries commensurate with responsibility and experience. Applications are accordingly invited from graduates in metallurgy, physics or chemistry. For the senior post, experience of either specialized information services or in the preparation and presentation of technical information is required. The junior post provides experience in methods of gathering and distributing information from world sources as well as training in editorial work.—Write Secretary, B.N.F.M.R.A., Euston Street, London, N.W.1.

WREXHAM, POWYS AND MAWDDACH HOSPITAL MANAGEMENT COMMITTEE

Applications are invited for the post of Hospital Biochemist (Senior Grade), to take charge of a newly built Department of Biochemistry at the Group Laboratory, Maelor General Hospital, Wrexham. Salary scale will be according to the new Whitley Council rates, i.e., £1,250 to £1,700 per annum.

Candidates with appropriate qualifications and experience should apply, giving full details of previous employment and the names of three referees to the undersigned by January 31, 1961.

WILLIAM JONES,
Group Secretary.

Maelor General Hospital,
Croesnewydd Road,
Wrexham, Denbighshire.

ADMINISTRATIVE ASSISTANT

Administrative assistant required by The Royal Society in connection with international scientific co-operation, particularly for Space and Antarctic research. Some experience in committee work would be an advantage. Salary according to age and qualifications in the range £950 to £1,650. Pension fund, luncheon vouchers, four weeks' annual leave.

Apply in writing to the Assistant Secretary, The Royal Society, Burlington House, Piccadilly, London, W.1, giving full details of age, qualifications and experience.

ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY

GLASGOW

(Affiliated to the University of Glasgow)

CHAIR OF PHARMACY

The Governors of the Royal College of Science and Technology invite applications for the Chair of Pharmacy which will fall vacant on the retirement of Professor J. P. Todd from September 1, 1961.

Further particulars may be obtained from the Secretary, George Street, Glasgow, C.1.

PEA GROWING RESEARCH ORGANIZATION LTD.

Applications are invited, not later than February 3, from male graduates in agriculture, or related subject, for the following posts: (1) Senior Technical Officer. Commencing salary up to £1,000 per annum. (2) Technical Officer. Commencing salary up to £700 per annum.

Further particulars and application forms may be obtained from the Secretary, Pea Research Station, Yaxley, Peterborough.

UNIVERSITY OF BELFAST

The Senate of the Queen's University of Belfast invites applications for a Lectureship in Light Electrical Engineering from October 1, 1961. Salary range £1,050 to £1,850 plus contributory pension rights under the F.S.S.U. Initial placing on the salary scale will depend on qualifications and experience.

Applications should be received by March 15, 1961. Further particulars may be obtained from G. R. Cowie, M.A., LL.B., J.P., Secretary.

SCIENCE GRADUATE REQUIRED FOR work in the Disinfection Reference Laboratory, Public Health Laboratory Service. Should have experience in chemical engineering, microbiology or biochemistry—ability to design apparatus and work out new techniques an advantage.—Apply the Acting Director, Central Public Health Laboratory, Colindale Avenue, London, N.W.9.

ASSISTANT EXPERIMENTAL OFFICER required in Statistics Section for work on the planning and analysis of experiments. Degree required in pure or applied biology with "A" level mathematics or degree in mathematics. Salary scale £645 (age 23) to £745 (age 26 or over), rising to £945 maximum (increase pending). Superannuation.—Apply with fullest particulars and names of two referees to the Secretary, Glasshouse Crops Research Institute, Worthing Road, Rustington, Littlehampton, Sussex, within three weeks.

THE AGRICULTURAL RESEARCH Council require an Assistant Experimental Officer/Experimental Officer (unestablished) for abstracting scientific literature in the field of post harvest storage problems. The appointment will be in the Tropical Liaison Department of the Pest Infestation Laboratory, London Road, Slough, Bucks. The salary scale for Assistant Experimental Officer is £458 to £983; for Experimental Officer, £1,087 to £1,336. Point of entry according to age and experience.—For further details apply to the Director.

STOKE MANDEVILLE HOSPITAL

AYLESBURY

Assistant Biochemist required in the Area Pathology Laboratory based at the above Hospital. Applicants should possess first- or second-class honours degree in chemistry or biochemistry, or A.R.I.C. Whitley Council conditions of service. Salary £925 to £1,150 per annum after (for new entrants only) a probationary period. The post offers a wide variety of experience in a well-equipped and pleasant laboratory.

Applications, giving full details of qualifications etc., together with names of two referees, to be forwarded to the Administrative Officer as soon as possible.

UNIVERSITY OF CAMBRIDGE

I.C.I. FELLOWSHIPS

Applications are invited for Imperial Chemical Industries Fellowships, value within the range £800 to £1,100 a year, tenable in the University and available for research in physics, chemistry, colloid science, biochemistry, engineering, metallurgy, pharmacology, chemotherapy, or related subjects.

Applications must be received not later than April 29, 1961. Regulations governing the award of the Fellowships may be obtained from the Secretary General of the Faculties, the Old Schools, Cambridge, to whom all applications should be addressed.

A SENIOR MICROBIOLOGIST IS REquired at Worthing to take charge of the Microbiological Laboratory associated with Antibiotic Production. Applicants should be qualified, and preferably have had previous experience of Microbiological Assay methods, sterility testing, and culture maintenance techniques.

Good salary, non-contributory pensions, and staff profit sharing schemes in operation.

Apply in writing, giving details of age, qualifications and experience, to Personnel Officer, Beecham Research Laboratories Ltd., Clarendon Road, Worthing, Sussex.

NIGER DAMS PROJECT

Organization engaged in investigating a major dam project on the Niger requires an Entomologist to take full charge of the local control of insects of medical importance, of which the first priority must be given to *Simulium damnosum*. Previous practical field experience essential. Salary £2,500 to £3,000 per annum, according to qualifications and experience. Contract for one tour of 12 to 18 months in the first instance. Free passages and accommodation with free board or allowance in lieu thereof. Kit allowance of £50.

Write Box F.213, Streets, Old Broad Street, London, E.C.2.

UNIVERSITY OF LONDON

READERSHIP IN MICROBIOLOGY AT QUEEN ELIZABETH COLLEGE

The Senate invites applications for the Readership in Microbiology tenable at Queen Elizabeth College (salary scale £1,675 to £1,975 to £2,425 a year plus £80 London allowance).

Applications (ten copies), must be received not later than February 21, 1961, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF GLASGOW

ASSISTANTSHIPS IN MATHEMATICS AND STATISTICS

Applications are invited for two Assistantships one in Mathematics and one in Statistics. Salary scale: £800 to £950 per annum. F.S.S.U. and family allowance benefits.

Applications (three copies) should be lodged not later than February 28, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court

VIROLOGIST AND CHIEF TECHNICIAN. We are looking for a man aged 30 to 40 with degree or F.I.M.L.T., to pioneer the application of new techniques to the diagnosis of poultry virus diseases. He should be able to organize his own work and supervise the other activities of a diagnostic laboratory. Experience with tissue culture an advantage. Knowledge of poultry not necessary. Starting salary according to age, experience and qualifications £1,100 to £1,600 per annum. Pension scheme.—Write to the Veterinary Surgeon, the Buxted Chicken Co., Ltd., Uckfield, Sussex.

UNIVERSITY OF LEICESTER

LECTURESHIP IN PHYSICS

Applications are invited for a Lectureship in Physics. Salary scale: £1,050 to £1,850 a year, with F.S.S.U. and family allowances; initial salary dependent on qualifications and experience.

Particulars from the Registrar, to whom applications should be sent by February 10.

McMASTER UNIVERSITY

POST-DOCTORAL FELLOWSHIPS IN PHYSICS

Applications are invited for National Research Council and other Post-Doctoral Fellowships, tenable in the Department of Physics, McMaster University. Successful applicants may choose to work full-time on their research or to supplement their research with a modest amount of lecturing.

Inquiries and applications should be addressed to Professor H. E. Duckworth, Chairman, Department of Physics, McMaster University, Hamilton, Ontario, Canada.

EXETER COLLEGE

OXFORD

The College proposes to elect an official Fellow and Lecturer in Mathematics. Applications are invited from mathematicians whose interests lie in the field of theoretical physics. The Fellow and Lecturer will be required to give instruction in Mathematics in the Honours Schools of Mathematics and of Natural Science (Physics). He would be expected to take up his duties, if possible, on October 1, 1961.

Information concerning emoluments and duties can be obtained on application to the Rector, Exeter College, Oxford, to whom applications, giving the names of three referees, should be sent not later than Saturday, February 25, 1961.

LABORATORY TECHNICIAN WITH EXperience of Biochemistry and preferably in Histology required for research on problems of bone metabolism to be carried out at the Group Laboratory, St. Mary Abbots Hospital, W.8. Salary according to qualifications and experience. —Detailed applications, naming two referees, to Hospital Secretary.

RESEARCH ASSISTANT WANTED AT Stoke Mandeville Hospital for immunological work. The person appointed would work directly with the pathologist undertaking the research. Immunological background and a knowledge of serological techniques desirable. Salary £750 to £1,000 per annum according to qualifications.—Inquiries and applications, giving details of experience and the names of two referees, to the Pathologist, Stoke Mandeville Hospital, Aylesbury, Bucks.

JUNIOR VACUUM TECHNOLOGIST needed to operate small diffusion pump section. Should be capable of working alone without constant supervision.—Apply RIChmond (Surrey) 6431, WB/J.V.T.

EAST MALLING RESEARCH STATION. Vacancy, Assistant Pomologist, Experimental Officer class, for experiments in fruit plant propagation. Horticultural degree or equivalent. Salary according to age and qualifications. Superannuation.—Details and application forms from Secretary, East Malling Research Station, Maidstone, Kent. Closing date, February 20.

FIELDSMAN. EXPERIENCED PERSON required before April 1 who will be responsible for the placing and supervision of the growing and harvesting of all our crops of Aberystwyth seeds, and advice to Representatives on leys, etc. A house is available. Pension Fund.—Please write in confidence to Managing Director, stating age, experience and salary required to: W. Sinclair and Son Limited, 35 Market Place, Boston, Lincolnshire.

PHYSICIST WITH ELECTRONIC AND/OR instrument experience, and preferably at least honours degree, required for fundamental and applied research in a growing organization concerned with building materials.—Write for form of application to Box No. 937, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

LECTURES AND COURSES

GRESHAM COLLEGE, BASINGHALL ST., London, E.C.2. Tel. MONarch 2433. Four lectures by Professor J. L. D'Silva, D.Sc., M.R.C.P. (Gresham Professor in Physic) on "The Nervous System," on Monday to Thursday, January 23 to 26.—The Lectures are free and begin at 5.30 p.m.

UNIVERSITY OF LEEDS

HOULDSWORTH SCHOOL OF APPLIED SCIENCE

POSTGRADUATE COURSE ON CERAMICS IN INDUSTRY

APRIL 10 TO MAY 10, 1961

A course of up to five weeks has been arranged for graduates and others of equivalent standing who are entering or are already working in the field of industrial ceramics, either as manufacturers or users. The subjects of lectures, discussions and demonstrations will include silica mineralogy, durability of refractories in service, clay mineralogy and clay-water relationships, basic refractories, and principles of design and operation of kilns and furnaces. Fee 25 guineas (or 7 guineas for each section taken separately). Reduced rates for members of teaching institutions.

Further particulars from the Department of Extra-Mural Studies, the University, Leeds 2.

IMPERIAL COLLEGE

DEPARTMENT OF CHEMICAL ENGINEERING

Course of twelve lectures will be given by Dr. K. E. Weale and Dr. K. E. Bett on "Polymerization at High Pressures" and "The Design of High Pressure Laboratory Equipment." Two lectures will be given every Thursday afternoon, beginning at 2.30 p.m. on February 9, 1961.

Applications to the Registrar, Imperial College London, S.W.7.

BRADFORD INSTITUTE OF TECHNOLOGY

DEPARTMENT OF CHEMICAL TECHNOLOGY

A Short Course on "Developments in the Use of Polymers and Plastics in Surface Coatings" will be held on Friday, February 24 and Saturday, February 25, 1961. Fee for the Course: £2 5s.

Full particulars and forms of application may be obtained from the Registrar, Bradford Institute of Technology, Bradford 7.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

LONDON, S.W.7

A course of four postgraduate lectures on the "Oxidation of Unsaturated Compounds" will be given in the Department of Chemical Engineering and Chemical Technology by Mr. A. Fish, B.A., on Mondays at 2.30 p.m., commencing February 20, 1961.

Details from the Registrar.

TRADE ANNOUNCEMENTS

SILICA CONES AND SOCKETS, VITREOsil silica tubing, polished silica discs and glazed sheet always in stock.—Custom built silica/quartz apparatus from Jencons, The Silica Centre, Mark Road, Hemel Hempstead, Hertfordshire. Boxmoor 4641.

GRANTS & SCHOLARSHIPS

UNIVERSITY OF OXFORD

METALLURGICAL RESEARCH

Several Research Bursaries are offered for work in the Department of Metallurgy on various problems in Physical Metallurgy. The Bursars are expected to read for the Oxford D.Phil. degree, and the work provides valuable training and experience. The Bursaries are of the value equivalent to those of D.S.I.R. Research Studentships (at present £420 per annum tax free, plus approved fees).

Candidates should have a first- or good second-class honours degree in metallurgy, physics or chemistry and should apply as soon as possible to Professor W. Hume-Rothery, Department of Metallurgy, Parks Road, Oxford, from whom full details can be obtained. Applications can be received from those graduating in the Summer of 1961, and those appointed will be expected to begin work on October 1.

NATO GRANTS

for participation in the CANADIAN THEORETICAL PHYSICS SEMINAR

Two grants of value $750 (£268) each are being offered by the North Atlantic Treaty Organization on a competitive basis to students of theoretical physics from NATO countries to attend the Second Quadriennial Theoretical Physics Seminar of the Canadian Association of Physicists to be held August 13 to September 9 at the University of Montreal. The seminar features lecture series by outstanding theoretical physicists as well as informal discussion on physics.

For further information and application forms write Dr. D. D. Betts, Department of Physics, University of Alberta, Edmonton, Canada. Deadline for applications is April 15.

UNIVERSITY OF WESTERN ONTARIO

LONDON, CANADA

DEPARTMENT OF CHEMISTRY

Demonstratorships, Research Assistantships, Scholarships, Fellowships, Bursaries, and Studentships, of value up to $2,800, are available for students working for the Ph.D. degree. Post-doctoral awards are available from $4,700. Excellent research facilities are on hand.

Inquiries, giving major field of interest, should be addressed to Professor F. L. M. Pattison, Head, Department of Chemistry, University of Western Ontario, London, Ontario, Canada.

UNIVERSITY OF LEEDS

THE FACULTIES OF SCIENCE, TECHNOLOGY AND MEDICINE

POSTGRADUATE SCHOLARSHIPS

Applications are invited for not more than three Postgraduate Research Scholarships tenable at the University of Leeds by graduates of other universities. These Scholarships, each of the value of £360 a year plus fees, will be tenable from October 1, 1961, for advanced study or research in the Faculties of Science, Technology and Medicine, and will be renewable annually. Maximum tenure three years.

Applications (including those of students who will graduate in June, 1961) should be submitted on forms obtainable from the Registrar, the University, Leeds, 2. Closing date May 1, 1961.

CHURCHILL COLLEGE

CAMBRIDGE

RESEARCH AND POSTGRADUATE STUDENTSHIPS

Churchill College offers the following Studentships, to commence in October, 1961, for qualified male candidates from the United Kingdom and overseas:

(a) One Research Studentship for men who intend to proceed to the degree of Ph.D. of the University of Cambridge.

(b) One Gulbenkian Studentship for men who intend to proceed to the degree of Ph.D. of the University of Cambridge and who are graduates of universities other than those in the United Kingdom; graduates of such universities, who have subsequently taken a degree in the United Kingdom, are also eligible.

(c) One Postgraduate Studentship for men who intend to pursue approved courses leading to Certificates of Postgraduate Study or Certificates of Advanced Study or certain Diplomas* of the University of Cambridge.

The elections will take place in May, 1961. The Research Studentships will normally be tenable for three years and the Postgraduate Studentships for one year. The value will be determined by the College Council after considering the Student's income from other studentships or grants, and will not exceed £465 a year in addition to the payment by the College of approved College and University fees.

Further particulars can be obtained from the Tutor for Advanced Students, Churchill College, Cambridge. Applications for Studentships must be received before April 1, 1961.

*The Diploma in Mathematical Statistics. The Diploma in Numerical Analysis and Automatic Computing. The Diploma in Economics.

COURTAULDS' SCIENTIFIC AND EDUCATIONAL TRUST FUND

POSTGRADUATE SCHOLARSHIPS

The Courtaulds' Scientific and Educational Trust Fund has been established with the object of encouraging study and research in those branches of natural science, including the cognate branches of engineering, which are likely to assist the textile, plastics and allied industries.

A limited number of Scholarships will be awarded in 1961 as follows:

Postgraduate Scholarships for research in a branch of science or technology which is related to the textile, plastics or allied industries. Preference will be given to candidates who will start their third year of research in October, 1961. The Scholarships are for a period of one year with a possibility of renewal in special cases for a second year and are tenable at any University or other approved educational establishment in the United Kingdom or abroad. The value of the Scholarships will be decided by the electors but will not exceed the sum of £475 per annum, inclusive of fees. For students at Oxford or Cambridge, a supplementary payment of £50 a year will be made.

The closing date for applications is February 11, 1961.

Forms of application are available from:

The Secretary,
Courtaulds' Scientific and Educational Trust Fund,
Courtaulds, Limited,
Foleshill Road,
COVENTRY.

McMASTER UNIVERSITY

GRADUATE SCHOLARSHIPS IN PHYSICS

Applications are invited for Graduate Scholarships in the Department of Physics, McMaster University, from students qualified to register in courses leading to the M.Sc. and Ph.D. degrees. These scholarships may be supplemented by Departmental Assistantships, requiring ten hours per week service during the seven-month academic year, to provide a yearly income (less fees) of $1,875 to $2,175.

Graduate Calendars and application forms for graduate study may be obtained from the Secretary of the Faculty of Graduate Studies. Further information concerning the types of research in progress and application forms for scholarships may be obtained from Professor H. E. Duckworth, Chairman, Department of Physics, Hamilton College, McMaster University, Hamilton, Ontario, Canada.

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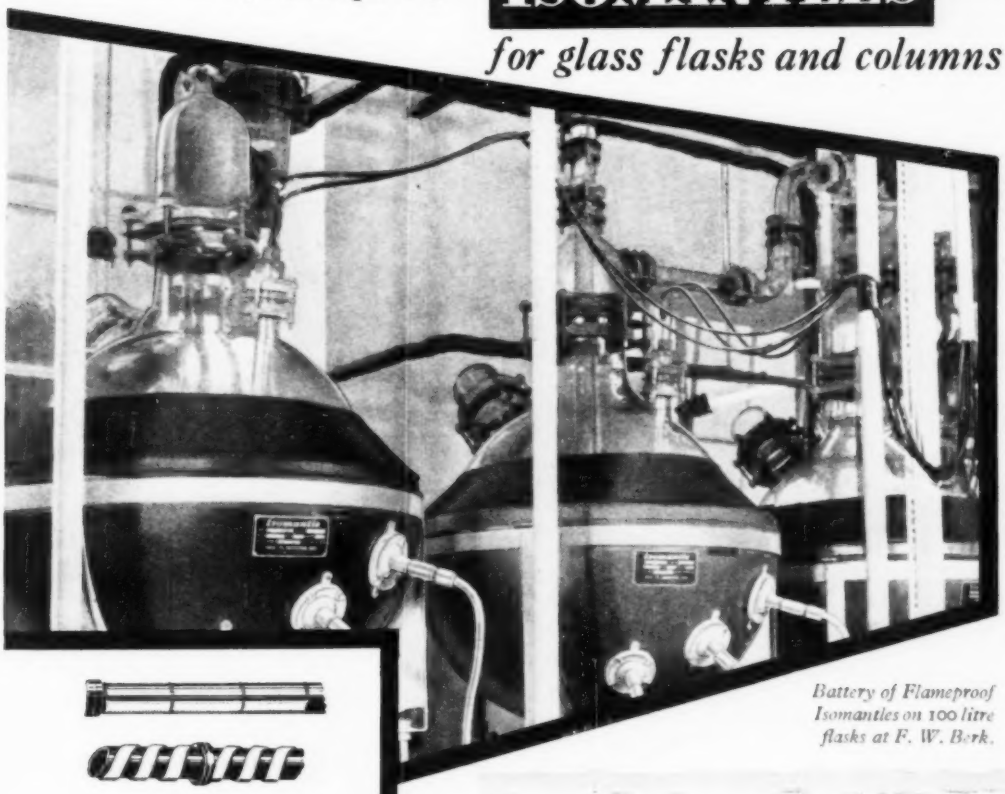

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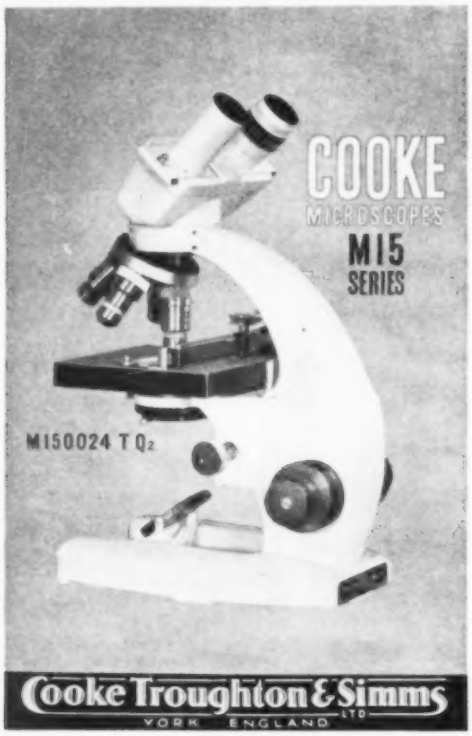

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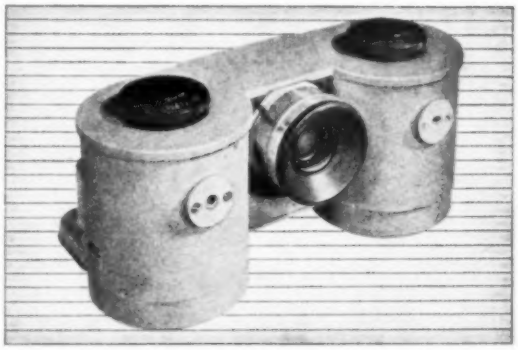

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ISOTOPIC TRENDS

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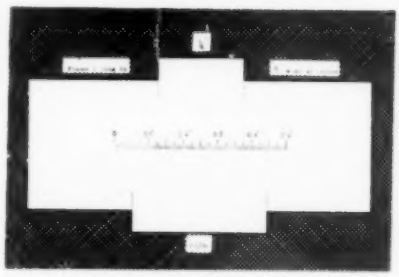
NOW AVAILABLE — The new Y Series Counting Mask for textiles, printing, etc. Frame in anodised black finish.

Just two of the many patterns available— Ref. Z.3 and Y.2



PATTERNS AVAILABLE:

Y Series Counting mask giving gaps of 1", ½", ¼" and 1 cm., combined with micrometer.

Ref. Y.1. 10 mm. in 100 parts.
Ref. Y.2. ¼" in 100 parts.

Z Series The field of view is 1" square.

Ref. Z.1. Micrometer 12 mm. in 120 parts.
Ref. Z.2. Micrometer ½" in 100 parts.
Ref. Z.3. Horizontal and vertical micrometer scales crossing in the centre, 10 mm. in 100 parts.
Ref. Z.4. As Z.3, but ½" in 100 parts.
Ref. Z.5. Concentric circles with numbered keyway, ½ to 12 mm. diameter.
Ref. Z.6. As Z.5, but 1/64" to 3/8".
Ref. Z.7. 100 1 mm. squares, one subdivided into 0.2 mm. side squares.
Ref. Z.8. 1 mm. squares all over.
Ref. Z.9. Half circle protractor with 12 mm. in 120 parts and foot scale.
Ref. Z.10. Globe and circle for particle analysis.

PRICES: Y Series 70/- each. Z Series 80/- each.

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